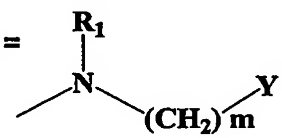
NOVEL HETEROCYCLIC COMPOUNDS

FIELD OF INVENTION

The present invention relates to novel hypolipidemic and hypocholesterolemic compounds, their tautomeric forms, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and pharmaceutically acceptable compositions containing them. More particularly, the present invention relates to novel heterocycle containing amino acid derivatives of the general formula (I), their tautomeric forms, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates, pharmaceutical compositions containing them, use of these compounds in medicine and the intermediates involved in their preparation.

(I)

G =



The present invention also relates to a process for the preparation of the above said novel compounds, their tautomeric forms, their pharmaceutically acceptable salts, and pharmaceutical compositions containing them.

The compounds of the general formula (I) lower or modulate triglyceride levels and/or cholesterol levels and/or low-density lipoproteins (LDL) and often raise HDL plasma levels and hence are useful in combating different medical conditions, where such lowering (and raising) is beneficial. Thus, it could be used in the treatment and/or prophylaxis of obesity, hyperlipidaemia, hypercholesteremia, hypertension, and atherosclerotic disease events. These compounds are also useful in the prophylaxis or treatment of diseases where insulin resistance is the underlying pathophysiological mechanism such as impaired glucose tolerance, diabetes, obesity, hyperlipidemia etc.

BACKGROUND OF THE INVENTION

The present invention discloses compounds suitable for the treatment of hyperlipidemia, diabetes, obesity and similar diseases by modulating the Peroxisome

Proliferator Activated Receptor (PPAR). The disease conditions, pathophysiology of the disease conditions, their effects and known & proposed therapies have been described in detail in WO 9119702, WO 9401420, WO 9413650, WO 9503038, WO 9517394, WO 9604260, WO 9604261, WO 9633998, WO 9725042, WO 9736579, WO 9828534, WO 9908501, WO 9916758, WO 9919313, WO9920614, WO 0023417, WO 0023445, WO 0023451, WO 0309841, WO 0066572, WO 0116111, WO 0116120, WO 0153257 etc. which are incorporated in their entirety as reference.

Hyperlipidemia has been recognized as the major risk factor in causing cardiovascular diseases due to atherosclerosis [*MetS Insights*, Sep; 4, 13-17 (2004)]. Atherosclerosis and other such peripheral vascular diseases affect the quality of life of a large population in the world. The therapy aims to lower the elevated plasma LDL cholesterol, low-density lipoprotein and plasma triglycerides in order to prevent or reduce the risk of occurrence of cardiovascular diseases. The detailed etiology of atherosclerosis and coronary artery diseases is discussed by Ross and Glomset [New Engl. J. Med., 295, 369-377 (1976)].

Peroxisome Proliferator Activated Receptor (PPAR) is a member of the steroid/ retinoid/ thyroid hormone receptor family. PPARα, PPARγ and PPARδ have been identified as subtypes of PPARs. The role of PPAR, in different disease conditions is widely established PPARγ activation has been found to play a central role in initiating and regulating adipocyte differentiation [Endocrinology 135, 798-800, (1994)] and energy homeostasis, [*Cell*, 83, 803-812 (1995); *Cell*, 99, 239-242 (1999)]. PPARγ agonists would stimulate the terminal differentiation of adipocyte precursors and cause morphological and molecular changes characteristic of a more differentiated, less malignant state. During adipocyte differentiation, several highly specialized proteins are induced, which are being involved in lipid storage and metabolism. It is accepted that PPARγ activation leads to expression of CAP gene [Cell Biology, 95, 14751-14756, (1998)], however, the exact link from PPARγ activation to changes in glucose metabolism and decrease in insulin resistance in muscle has not been clear. PPARα is involved in stimulating β-oxidation of fatty acids [*Trends Endocrine. Metabolism*, 4, 291-296 (1993)] resulting in plasma circulating free fatty acid reduction [*Current Biol.*, 5, 618-621 (1995)]. The role of PPARs in regulation of obesity-related insulin sensitivity and inflammation [*Int J Obes Relat*

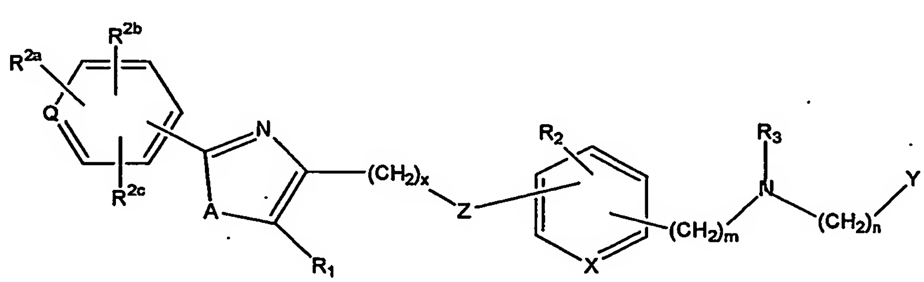
Metab Disord. Dec; 27 Suppl 3:S17-21(2003)], lipid metabolism and insulin sensitivity [*Diabetes* Feb;53 Suppl 1:S43-50 (2004)] have been fairly well established. PPARs are also believed to play a role in diseases associated with metabolic syndrome [*Curr Top Med Chem.*, 3(14): 1649-61(2003)]. There is growing evidence that PPAR agonists may also influence the cardiovascular system through PPAR receptors as well as directly by modulating vessel wall function [*Diabetes Metab.*, Feb; 30(1): 7-12 (2004); *Drugs Today (Barc)*, Dec;39(12):949-60 (2003)].

PPAR agonists have been found useful in the treatment of obesity [WO 97/36579; *Nat Med.*, Apr; 10(4):355-61(2004)]. Dual PPAR α and γ agonists have been suggested to be useful for Syndrome X (WO 97/25042). PPAR γ agonists and HMG-CoA reductase inhibitors have exhibited synergism and indicated the usefulness of the combination in the treatment of atherosclerosis and xanthoma [EP 0753 298; *Cardiol Rev.* May-Jun; 12(3): 158-70 (2004)].

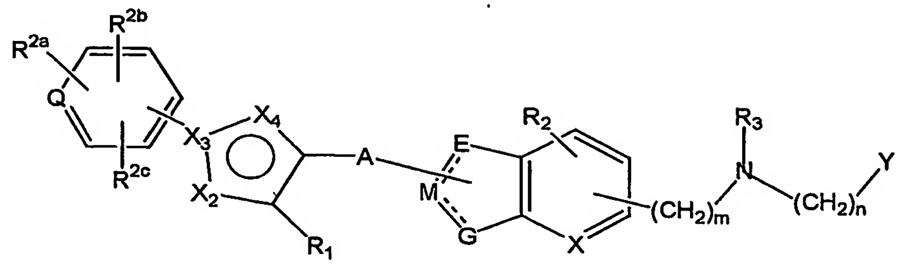
Leptin is a protein when bound to leptin receptors is involved in sending satiety signal to the hypothalamus. Leptin resistance would therefore lead to excess food in-take, reduced energy expenditure, obesity, impaired glucose tolerance and diabetes [*Science*, 269, 543-46(1995); *Recent Prog Horm Res.*, 59: 169-205 (2004); *Ann N Y Acad Sci*, Jun; 967: 363-78 (2002)]. It has been reported that insulin sensitizers lower plasma leptin concentration [*Proc. Natl. Acad. Sci.* 93, 5793-5796 (1996); WO 98/02159].

A few compounds belonging to the class of heterocycle containing amino acid derivatives have been reported to be useful in the treatment of hyperlipidemia, hypercholesterolemia, antiobesity and hyperglycemia which includes those described in

i) US 6414002 (Cheng et al.) which discloses compounds of the following general formula



ii) WO 0340114 A1 (Devasthale et al.) which discloses compounds having the following general formula

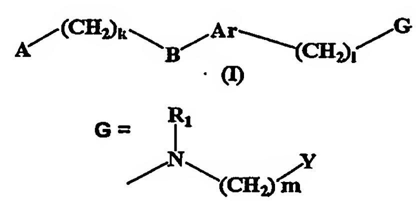


which are incorporated in their entirety as reference.

However, none of them have been commercialized so far. There is always an unmet medical need to provide better and cost effective medicines which are better than or of comparable efficacy with the present treatment regimes, and also having a better patient compliant regime.

SUMMARY OF THE INVENTION

The present invention thus provides new compounds of general formula (I)



their tautomeric forms, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and pharmaceutically acceptable compositions containing them and their use in medicine. The present invention also discloses a process for the preparation of compounds of formula (I) and pharmaceutical compositions containing them.

OBJECTS OF THE INVENTION

It is an object of this invention is to develop novel compounds represented by the general formula (I) useful for the treatment of hypocholesterolemia, hyperlipidemia, hypoalphalipoproteinemia, obesity, hyperglycemia, hypertriglyceridemia, diabetes mellitus, which may have additional body weight lowering effect and beneficial effect in the treatment and/or prophylaxis of diseases caused by hyperlipidaemia, diseases classified under syndrome X and atherosclerosis.

Another object of the present invention is to provide novel heterocycle containing amino acid derivatives represented by general formula (I), their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and pharmaceutical compositions containing them or their mixtures thereof and their use in medicine.

Yet another object of this invention is to provide processes for the preparation of novel heterocycle containing amino acid derivatives represented by the general formula (I), their analogs, their tautomeric forms and their pharmaceutically acceptable salts or solvates.

Still another object of the present invention is to provide pharmaceutical compositions containing compounds of the general formula (I), their analogs, their tautomeric forms, their pharmaceutically acceptable salts or their mixtures in combination with suitable carriers, solvents, diluents and other media normally employed in preparing such compositions.

A further object of the present invention is to provide processes for preparation of intermediates involved in the preparation of compounds of formula (I).

DETAILED DESCRIPTION OF THE INVENTION

Accordingly, the present invention relates to compounds of the general formula (I),

(I)

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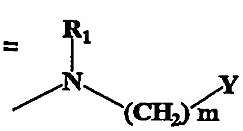


their tautomeric forms, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates wherein

'A' represents an optionally substituted group selected from aryl, heteroaryl, heterocyclyl groups, each of them may optionally be fused, wherein when 'A' is substituted, suitable substituents may be selected from hydroxyl, oxo, halo, thio, nitro, amino, cyano, formyl, alkyl, haloalkyl, perhaloalkyl, alkoxy, haloalkoxy, perhaloalkoxy, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, bicycloalkyl, bicycloalkenyl, alkoxy, alkenoxy, cycloalkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocylyl, heteroaryl, heterocyclylalkyl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, heterocyclylalkoxy, heterocyclylalkoxyacyl, acyl, acyloxy, acylamino, monosubstituted or disubstituted amino, arylamino, aralkylamino, carboxylic acid and its derivatives such as esters and amides, carbonylamino, hydroxyalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl, arylthio, alkylsulfonylamino, alkylsulfonyloxy, alkoxycarbonylamino, aryloxycarbonylamino, aralkyloxycarbonylamino, aminocarbonylamino, alkylaminocarbonylamino, alkoxyamino, hydroxyl amino, sulfenyl derivatives, sulfonyl derivatives, sulfonic acid derivatives;

'B' represents oxygen or sulfur; 'Ar' represents an optionally substituted divalent aromatic, heteroaromatic or a heterocyclic group, each of them may optionally be fused, wherein when 'Ar' is substituted, suitable substituents may be selected from optionally substituted linear or branched alkyl, alkoxy, thioalkyl, halogen, haloalkyl, haloalkoxy, acyl, amino, acylamino, thio or carboxylic acid derivatives or sulfonic acids or their derivatives;

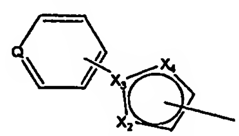
R_1 represents hydrogen, optionally substituted groups selected from alkyl (linear or branched), alkenyl (linear or branched), alkynyl (linear or branched), aralkyl, aryloxycarbonyl, alkoxycarbonyl, alkynyloxycarbonyl, alkenyloxycarbonyl, arylcarbonyl, alkylcarbonyl, aryl, heteroaryl, heteroarylcarbonyl, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, heteroaryloxycarbonylamino, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, heteroaryloxycarbonyl, heterocyclyloxycarbonyl, alkylaminocarbonyl, arylaminocarbonyl, hydroxyalkyl, alkoxy, alkylsulfonyl, arylthiocarbonyl, heteroarylsulfonyl, arylsulfonyl groups;

when R_1 is substituted, the substituents may be selected from hydroxyl, oxo, halo, thio, nitro, amino, cyano, formyl, alkyl, haloalkyl, perhaloalkyl, alkoxy, haloalkoxy,

perhaloalkoxy, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, bicycloalkyl, bicycloalkenyl, alkoxy, alkenoxy, cycloalkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocylyl, heteroaryl, heterocyclylalkyl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, heterocyclylalkoxy, heterocyclylalkoxyalkyl, heterocyclylalkoxyacyl, acyl, acyloxy, acylamino, monosubstituted or disubstituted amino, arylamino, aralkylamino, carboxylic acid and its derivatives such as esters and amides; k, l and m are integers independently ranging from 1-3; Y is COR_3 (where R_3 is OH or substituted or unsubstituted alkoxy, aryloxy, aralkyloxy, NH_2, aminoalkyl, amiodialkyl, aminoaralkyl, aminoalkylaralkyl groups);

$(CH_2)_k$, $(CH_2)_l$, $(CH_2)_m$, may be optionally substituted with one or more substituents selected from optionally substituted alkyl, haloalkyl, aryl, alkenyl, alkoxy, aryloxy, aralkoxy, alkoxycarbonyl, aryloxycarbonyl and the like;

with the proviso that, 'A' does not represent



where Q is 'C' or 'N' and X_2, X_3 & X_4 are independently selected from C, N, O or S;

The various groups, radicals and substituents used anywhere in the specification are described in the following paragraphs.

The term "alkyl" used herein, either alone or in combination with other radicals, denotes a linear or branched radical containing one to twelve carbons, such as methyl, ethyl, *n*-propyl, *iso*-propyl, *n*-butyl, *sec*-butyl, *tert*-butyl, amyl, *t*-amyl, *n*-pentyl, *n*-hexyl, *iso*-hexyl, heptyl, octyl and the like.

The term "alkenyl" used herein, either alone or in combination with other radicals, denotes a linear or branched radical containing two to twelve carbons such as vinyl, allyl, 2-butenyl, 3-butenyl, 2-pentenyl, 3-pentenyl, 4-pentenyl, 2-hexenyl, 3-hexenyl, 4-hexenyl, 5-hexenyl, 2-heptenyl, 3-heptenyl, 4-heptenyl, 5-heptenyl, 6-heptenyl and the like. The term "alkenyl" includes dienes and trienes of straight and branched chains.

The term "alkynyl" used herein, either alone or in combination with other radicals, denotes a linear or branched radical containing two to twelve carbons, such as ethynyl, 1-propynyl, 2-propynyl, 1-butynyl, 2-butynyl, 3-butynyl, 1-pentynyl, 2-pentynyl, 3-pentynyl,

4-pentynyl, 1-hexynyl, 3-hexynyl, 4-hexynyl, 5-hexynyl, and the like. The term "alkynyl" includes di- and tri-ynes.

The term "cycloalkyl" used herein, either alone or in combination with other radicals, denotes a radical containing three to seven carbons, such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and the like.

The term "cycloalkenyl" used herein, either alone or in combination with other radicals, denotes a radical containing three to seven carbons, such as cyclopropenyl, 1-cyclobutenyl, 2-cylobutenyl, 1-cyclopentenyl, 2-cyclopentenyl, 3-cyclopentenyl, 1-cyclohexenyl, 2-cyclohexenyl, 3-cyclohexenyl, 1-cycloheptenyl, cycloheptadienyl, cycloheptatrienyl, and the like.

The term "alkoxy" used herein, either alone or in combination with other radicals, denotes an alkyl radical, as defined above, attached directly to an oxygen atom, such as methoxy, ethoxy, *n*-propoxy, *iso*-propoxy, *n*-butoxy, *t*-butoxy, *iso*-butoxy, pentyloxy, hexyloxy, and the like.

The term "alkenoxy" used herein, either alone or in combination with other radicals, denotes an alkenyl radical, as defined above, attached to an oxygen atom, such as vinyloxy, allyloxy, butenoxy, pentenoxy, hexenoxy, and the like.

The term "cycloalkoxy" used herein, either alone or in combination with other radicals, denotes a cycloalkyl radical as defined above, attached directly to an oxygen atom, such as cyclopropyloxy, cyclobutyloxy, cyclopentyloxy, cyclohexyloxy, cycloheptyloxy and the like.

The term "halo" or "halogen" used herein, either alone or in combination with other radicals, such as "haloalkyl", "perhaloalkyl" etc refers to a fluoro, chloro, bromo or iodo group. The term "haloalkyl" denotes an alkyl radical, as defined above, substituted with one or more halogens such as perhaloalkyl, preferably, perfluoro(C_1-C_6)alkyl such as fluoromethyl, difluoromethyl, trifluoromethyl, fluoroethyl, difluoroethyl, trifluoroethyl, mono or polyhalo substituted methyl, ethyl, propyl, butyl, pentyl or hexyl groups. The term "haloalkoxy" denotes a haloalkyl, as defined above, directly attached to an oxygen atom, such as fluoromethoxy, chloromethoxy, fluoroethoxy chloroethoxy groups, and the like. The term "perhaloalkoxy" denotes a perhaloalkyl radical, as defined above, directly attached to an oxygen atom, trifluoromethoxy, trifluoroethoxy, and the like.

The term "aryl" or "aromatic" used herein, either alone or in combination with other radicals, denotes an aromatic system containing one, two or three rings wherein such rings may be attached together in a pendant manner or may be fused, such as phenyl, naphthyl, tetrahydronaphthyl, indane, biphenyl, and the like. The term 'aralkyl" denotes an alkyl group, as defined above, attached to an aryl, such as benzyl, phenethyl, naphthylmethyl, and the like. The term "aryloxy" denotes an aryl radical, as defined above, attached to an alkoxy group, such as phenoxy, naphthyloxy and the like, which may be substituted. The term "aralkoxy" denotes an arylalkyl moiety, as defined above, such as benzyloxy, phenethyloxy, naphthylmethyloxy, phenylpropyloxy, and the like, which may be substituted.

The term "heterocyclyl" or "heterocyclic" used herein, either alone or in combination with other radicals, denotes saturated, partially saturated and unsaturated ring-shaped radicals containing one or more hetero atoms selected from nitrogen, sulfur and oxygen. Examples of saturated heterocyclic radicals include aziridinyl, azétidinyl, pyrrolidinyl, imidazolidinyl, piperidinyl, piperazinyl, 2-oxopiperidinyl, 4-oxopiperidinyl, 2-oxopiperazinyl, 3-oxopiperazinyl, morpholinyl, thiomorpholinyl, 2-oxomorpholinyl, azepinyl, diazepinyl, oxapinyl, thiazepinyl, oxazolidinyl, thiazolidinyl, and the like; examples of partially saturated heterocyclic radicals include dihydrothiophene, dihydropyran, dihydrofuran, dihydrothiazole, and the like.

The term "heteroaryl" or "heteroaromatic" used herein, either alone or in combination with other radicals, denotes aromatic radicals containing one or more hetero atoms selected from O, N, S or unsaturated 5 to 6 membered heterocyclic radicals containing one or more hetero atoms selected from O, N or S, attached to an aryl group, such as pyridyl, thienyl, furyl, pyrrolyl, oxazolyl, thiazolyl, isothiazolyl, imidazolyl, isoxazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, benzopyranyl, benzopyranonyl, benzofuranyl, benzothienyl, indolinyl, indolyl, quinolinyl, pyrimidinyl, pyrazolyl, quinazolinyl, quinazolonyl, pyrimidonyl, pyridazinyl, triazinyl, benzoxazinyl, benzoxazinonyl, benzothiazinyl, benzothiazinonyl, benzoxazolyl, benzothiazolyl, benzimidazolyl, benzotriazolyl, phthalazynil, naphthylidinyl, purinyl, carbazolyl, phenothiazinyl, phenoxazinyl, and the like.

The term "heterocyclylalkyl" used herein, either alone or in combination with other radicals, represents a heterocyclyl group, as defined above, substituted with an alkyl group of one to twelve carbons, such as pyrrolidinealkyl, piperidinealkyl, morpholinealkyl, thiomorpholinealkyl, oxazolinealkyl, and the like, which may be substituted. The term "heteroaralkyl" used herein, either alone or in combination with other radicals, denotes a heteroaryl group, as defined above, attached to a straight or branched saturated carbon chain containing 1 to 6 carbons, such as (2-furyl)methyl, (3-furyl)methyl, (2-thienyl)methyl, (3-thienyl)methyl, (2-pyridyl)methyl, 1-methyl-1-(2-pyrimidyl)ethyl and the like. The terms "heteroaryloxy", "heteroaralkoxy", "heterocycloxy", "heterocylylalkoxy" denotes heteroaryl, heteroarylalkyl, heterocyclyl, heterocylylalkyl groups respectively, as defined above, attached to an oxygen atom.

The term "acyl" used herein, either alone or in combination with other radicals, denotes a radical containing one to eight carbons such as formyl, acetyl, propanoyl, butanoyl, *iso*-butanoyl, pentanoyl, hexanoyl, heptanoyl, benzoyl and the like, which may be substituted.

The term "acyloxy" used herein, either alone or in combination with other radicals, denotes a radical acyl, as defined above, directly attached to an oxygen atom, such as acetyloxy, propionyloxy, butanoyloxy, *iso*-butanoyloxy, benzoyloxy and the like.

The term "acylamino" used herein, either alone or in combination with other radicals, denotes an acyl group as defined earlier, may be CH_3CONH, C_2H_5CONH, C_3H_7CONH, C_4H_9CONH, C_6H_5CONH and the like, which may be substituted.

The term "mono-substituted amino" used herein, either alone or in combination with other radicals, denotes an amino group, substituted with one group selected from (C_1-C_6)alkyl, substituted alkyl, aryl, substituted aryl or arylalkyl groups. Examples of monoalkylamino group include methylamine, ethylamine, *n*-propylamine, *n*-butylamine, *n*-pentylamine and the like.

The term 'disubstituted amino" used herein, either alone or in combination with other radicals, denotes an amino group, substituted with two radicals that may be same or different selected from (C_1-C_6)alkyl, substituted alkyl, aryl, substituted aryl, or arylalkyl groups, such as dimethylamino, methylethylamino, diethylamino, phenylmethyl amino and the like.

The term "arylamino" used herein, either alone or in combination with other radicals, denotes an aryl group, as defined above, linked through amino having a free valence bond from the nitrogen atom, such as phenylamino, naphthylamino, N-methyl anilino and the like.

The term "aralkylamino" used herein, either alone or in combination with other radicals, denotes an arylalkyl group as defined above linked through amino having a free valence bond from the nitrogen atom e.g. benzylamino, phenethylamino, 3-phenylpropylamino, 1-napthylmethylamino, 2-(1-napthyl)ethylamino and the like.

The term "oxo" or "carbonyl" used herein, either alone (-C=O-) or in combination with other radicals, such as "alkylcarbonyl", "alkoxycarbonyl", "arylcarbonyl", "aryloxycarbonyl", "heteroarylcarbonyl", "heteroaryloxycarbonyl", "heterocyclyloxycarbonyl" denotes a carbonyl radical (–C=O-) substituted with an alkyl, alkoxy, aryl, aryloxy, heteroaryl, heteroaryloxy, heterocyclyloxy radicals as described above.

The term "carboxylic acid" used herein, alone or in combination with other radicals, denotes a –COOH group, and includes derivatives of carboxylic acid such as esters and amides. The term "ester" used herein, alone or in combination with other radicals, denotes –COO- group, and includes carboxylic acid derivatives, where the ester moieties are alkoxycarbonyl, such as methoxycarbonyl, ethoxycarbonyl, and the like, which may be substituted; aryloxycarbonyl group such as phenoxycarbonyl, napthyloxycarbonyl, and the like, which may be substituted; aralkoxycarbonyl group such as benzyloxycarbonyl, phenethyloxycarbonyl, napthylmethoxycarbonyl, and the like, which may be substituted; heteroaryloxycarbonyl, heteroaralkoxycarbonyl, wherein the heteroaryl group, is as defined above, which may be substituted; heterocyclyloxycarbonyl, where the heterocyclic group, as defined earlier, which may be substituted.

The term "amide" used herein, alone or in combination with other radicals, represents an aminocarbonyl radical (H_2N-C=O-), wherein the amino group is mono- or di-substituted or unsubstituted, such as methylamide, dimethylamide, ethylamide, diethylamide, and the like. The term "aminocarbonyl" used herein, either alone or in combination with other radicals, with other terms such as 'aminocarbonylalkyl", "n-alkylaminocarbonyl", "N-arylaminocarbonyl", "N,N-dialkylaminocarbonyl", "N-alkyl-N-arylaminocarbonyl", "N-

alkyl-N-hydroxyaminocarbonyl", and "N-alkyl-N-hydroxyaminocarbonylalkyl", substituted or unsubstituted. The terms "N-alkylaminocabonyl" and "N,N-dialkylaminocarbonyl" denotes aminocarbonyl radicals, as defined above, which have been substituted with one alkyl radical and with two alkyl radicals, respectively. Preferred are "lower alkylaminocarbonyl" having lower alkyl radicals as described above attached to aminocarbonyl radical. The terms "N-arylaminocarbonyl" and "N-alkyl-N-arylaminocarbonyl" denote amiocarbonyl radicals substituted, respectively, with one aryl radical, or one alkyl, and one aryl radical. The term "aminocarbonylalkyl" includes alkyl radicals substituted with aminocarbonyl radicals.

The term "hydroxyalkyl" used herein, either alone or in combination with other radicals, denotes an alkyl group, as defined above, substituted with one or more hydroxy radicals, such as hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, hydroxypentyl, hydroxyhexyl and the like.

The term "aminoalkyl" used herein, alone or in combination with other radicals, denotes an amino ($-NH_2$) moiety attached to an alkyl radical, as defined above, which may be substituted, such as mono- and di-substituted aminoalkyl. The term "alkylamino" used herein, alone or in combination with other radicals, denotes an alkyl radical, as defined above, attached to an amino group, which may be substituted, such as mono- and di-substituted alkylamino.

The term "alkoxyalkyl" used herein, alone or in combination with other radicals, denotes an alkoxy group, as defined above, attached to an alkyl group, such as methoxymethyl, ethoxymethyl, methoxyethyl, ethoxyethyl and the like. The term "aryloxyalkyl" used herein, alone or in combination with other radicals, includes phenoxymethyl, napthyloxymethyl, and the like. The term "aralkoxyalkyl" used herein, alone or in combination with other radicals, includes $C_6H_5CH_2OCH_2$, $C_6H_5CH_2OCH_2CH_2$, and the like.

The term "alkylthio" used herein, either alone or in combination with other radicals, denotes a straight or branched or cyclic monovalent substituent comprising an alkyl group of one to twelve carbon atoms, as defined above, linked through a divalent sulfur atom having a free valence bond from the sulfur atom, such as methylthio, ethylthio, propylthio,

butylthio, pentylthio and the like. Examples of cyclic alkylthio are cyclopropylthio, cyclobutylthio, cyclopentylthio, cyclohexylthio and the like, which may be substituted.

The term "thioalkyl" used herein, either alone or in combination with other radicals, denotes an alkyl group, as defined above, attached to a group of formula –SR', where R' represents hydrogen, alkyl or aryl group, e.g. thiomethyl, methylthiomethyl, phenylthiomethyl and the like, which may be substituted.

The term "arylthio' used herein, either alone or in combination with other radicals, denotes an aryl group, as defined above, linked through a divalent sulfur atom, having a free valence bond from the sulfur atom such as phenylthio, napthylthio and the like.

The term "alkoxycarbonylamino" used herein, alone or in combination with other radicals, denotes an alkoxycarbonyl group, as defined above, attached to an amino group, such as methoxycarbonylamino, ethoxycarbonylamino, and the like. The term "aryloxycarbonylamino" used herein, alone or in combination with other radicals, denotes an aryloxycarbonyl group, as defined above, attached to the an amino group, such as C_6H_5OCONH, $C_6H_5OCONCH_3$, $C_6H_5OCONC_2H_5$, $C_6H_4(CH_3O)CONH$, $C_6H_4(OCH_3)OCONH$, and the like. The term "aralkoxycarbonylamino" used herein, alone or in combination with other radicals, denotes an aralkoxycarbonyl group, as defined above, attached to an amino group $C_6H_5CH_2OCONH$, $C_6H_5CH_2CH_2CH_2OCONH$, $C_6H_5CH_2OCONHCH_3$, $C_6H_5CH_2OCONC_2H_5$, $C_6H_4(CH_3)CH_2OCONH$, $C_6H_4(OCH_3)CH_2OCONH$, and the like.

The term "aminocarbonylamino", "alkylaminocarbonylamino", "dialkylaminocarbonylamino" used herein, alone or in combination with other radicals, denotes a carbonylamino (-$CONH_2$) group, attached to amino(NH_2), alkylamino group or dialkylamino group respectively, where alkyl group is as defined above.

The term "alkoxyamino" used herein, alone or in combination with other radicals, denotes an alkoxy group, as defined above, attached to an amino group. The term "hydroxyamino" used herein, alone or in combination with other radicals, denotes –NHOH moiety, and may be substituted.

The term "sulfenyl" or "sulfenyl and its derivatives" used herein, alone or in combination with other radicals, denotes a bivalent group, –SO- or R_nSO, where R_n is substituted or unsubstituted alkyl, aryl, heteroaryl, heterocyclyl, and the like.

The term "sulfonyl" or "sulfones and its derivatives" used herein, either alone or in combination with other radicals, with other terms such as alkylsulfonyl, denotes divalent radical $-SO_2-$, or R_nSO_2-, where R_n is substituted or unsubstituted groups selected from alkyl, aryl, heteroaryl, heterocyclyl, and the like. "Alkylsulfonyl" denotes alkyl radicals, as defined above, attached to a sulfonyl radical, such as methylsulfonyl, ethylsulfonyl, propylsulfonyl and the like. The term "arylsulfonyl" used herein, either alone or in combination with other radicals, denotes aryl radicals, as defined above, attached to a sulfonyl radical, such as phenylsulfonyl and the like.

The term "substituted" used in combination with other radicals including when used as substitutions on any of the substituents, denotes suitable substituents on that radical such as substituted alkyl, substituted alkenyl, substituted alkynyl, substituted cycloalkyl, substituted aryl, etc, mentioned anywhere in the specification. The suitable substituents include, but are not limited to the following radicals, alone or in combination with other radicals- hydroxyl, oxo, halo, thio, nitro, amino, cyano, formyl, alkyl, haloalkyl, perhaloalkyl, alkoxy, haloalkoxy, perhaloalkoxy, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, bicycloalkyl, bicycloalkenyl, alkoxy, alkenoxy, cycloalkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocylyl, heteroaryl, heterocyclylalkyl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, heterocyclylalkoxy, heterocyclylalkoxyalkyl, heterocyclylalkoxyacyl, acyl, acyloxy, acylamino, monosubstituted or disubstituted amino, arylamino, aralkylamino, carboxylic acid and its derivatives such as esters and amides, carbonylamino, hydroxyalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl, arylthio, alkoxycarbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, aralkyloxycarbonylamino, aminocarbonylamino, alkylaminocarbonylamino, dialkylaminocarbonylamino, alkoxyamino, hydroxyl amino, sulfenyl derivatives, sulfonyl derivatives.

Suitable groups and substituents on the groups may be selected from those described anywhere in the specification.

Particularly useful compounds according to the present invention includes

Ethyl-[4-(2-phenoxazin-10-yl-ethoxy)-benzylamino]-acetate;

Ethyl-[4-(2-phenothiazin-10-yl-ethoxy)-benzylamino]-acetate;

Methyl-[4-(2-oxo-3-phenyl-oxazolidin-5-ylmethoxy)-benzylamino]-acetate;

Ethyl-[(6-benzyloxy-naphthalen-2-ylmethyl)-amino]-acetate;

Ethyl-{[6-(1-phenyl-pentyloxy)-naphthalen-2-ylmethyl]-amino}-acetate;

Ethyl-[4-(2-carbazol-9-yl-ethoxy)-benzylamino]-acetate;

Ethyl-[4-(1-pyridin-2-yl-pyrrolidin-2-ylmethoxy)-benzylamino]-acetate;

Ethyl-{4-[2-(2,3-dihydro-benzo[1,4]oxazin-4-yl)-ethoxy]-benzylamino}-acetate;

Ethyl-(benzyl-{3-[2-(3,4-dihydro-2H-quinolin-1-yl)-ethoxy]-benzyl}-amino)-acetate;

Ethyl-(benzyl-{3-[2-(4-methanesulfonyloxy-phenyl)-ethoxy]-benzyl}-amino)-acetate;

Ethyl-(benzyl-{3-[2-(4-hydroxy-phenyl)-ethoxy]-benzyl}-amino)-acetate;

Ethyl-{benzyl-[3-(2-phenoxazin-10-yl-ethoxy)-benzyl]-amino}-acetate;

Ethyl-{benzyl-[3-(2-carbazol-9-yl-ethoxy)-benzyl]-amino}-acetate;

Ethyl-(benzyl-{3-[2-(5-ethyl-pyridin-2-yl)-ethoxy]-benzyl}-amino)-acetate;

Ethyl-(benzyl-{3-[2-(2,3-dihydro-benzo[1,4]oxazin-4-yl)-ethoxy]-benzyl}-amino)-acetate;

Ethyl-(benzyl-{3-[2-(2,3-dihydro-benzo[1,4]thiazin-4-yl)-ethoxy]-benzyl}-amino)-acetate;

Ethyl-{benzyl-[3-(2-indol-1-yl-ethoxy)-benzyl]-amino}-acetate;

Ethyl-{benzyl-[3-(3-phenothiazin-10-yl-propoxy)-benzyl]-amino}-acetate;

Ethyl-{benzyl-[3-(3-methyl-4-oxo-3,4-dihydro-quinazolin-2-ylmethoxy)-benzyl]-amino}-acetate;

Ethyl-[benzyl-(3-{2-[2-methyl-5-(4-methylsulfanyl-phenyl)-pyrrol-1-yl]-ethoxy}-benzyl)-amino]-acetate;

Ethyl-{benzyl-[3-(2-oxo-3-phenyl-oxazolidin-5-ylmethoxy)-benzyl]-amino}-acetate;

Ethyl-{(4-methoxy-phenoxycarbonyl)-[4-(2-phenoxazin-10-yl-ethoxy)-benzyl]-amino}-acetate;

Ethyl-{(4-methoxy-phenoxycarbonyl)-[4-(2-phenothiazin-10-yl-ethoxy)-benzyl]-amino}-acetate;

Methyl-{(4-methoxy-phenoxycarbonyl)-[4-(2-oxo-3-phenyl-oxazolidin-5-ylmethoxy)-benzyl]-amino}-acetate;

Ethyl-[(6-benzyloxy-naphthalen-2-ylmethyl)-(4-methoxy-phenoxycarbonyl)-amino]-acetate;

Methyl-{(4-methoxy-phenoxycarbonyl)-[6-(1-phenyl-pentyloxy)-naphthalen-2-ylmethyl]-amino}-acetate;

Ethyl-[{4-[2-(6,7-dihydro-4H-thieno[3,2-c]pyridin-5-yl)-ethoxy]-benzyl}-(4-methoxy-phenoxycarbonyl)-amino]-acetate;

Ethyl-[{4-[2-(2,3-dihydro-benzo[1,4]thiazin-4-yl)-ethoxy]-benzyl}-(4-methoxy-phenoxycarbonyl)-amino]-acetate;

Ethyl-[[4-(2-indol-1-yl-ethoxy)-benzyl]-(4-methoxy-phenoxycarbonyl)-amino]-acetate;

Ethyl-[[4-(2-carbazol-9-yl-ethoxy)-benzyl]-(4-methoxy-phenoxycarbonyl)-amino]-acetate;

Ethyl-{(4-methoxy-phenoxycarbonyl)-[4-(1-pyridin-2-yl-pyrrolidin-2-ylmethoxy)-benzyl]-amino}-acetate;

Ethyl-[{4-[2-(2,3-dihydro-benzo[1,4]oxazin-4-yl)-ethoxy]-benzyl}-(4-methoxy-phenoxycarbonyl)-amino]-acetate;

Ethyl-(ethoxycarbonylmethyl-{4-[2-(5-methyl-2-phenyl-oxazol-4-yl)-ethoxy]-benzyl}-amino)-acetate;

Ethyl-(benzyl-{4-[2-(5-methyl-2-thiophen-2-yl-oxazol-4-yl)-ethoxy]-benzyl}-amino)-acetate;

Ethyl-(benzyl-{3-[2-(5-methyl-2-thiophen-2-yl-oxazol-4-yl)-ethoxy]-benzyl}-amino)-acetate;

Ethyl-[benzyl-(4-{2-[2-methyl-5-(4-methylsulfanyl-phenyl)-pyrrol-1-yl]-ethoxy}-benzyl)-amino]-acetate;

Ethyl-(benzyl-{4-[2-(methyl-pyridin-2-yl-amino)-ethoxy]-benzyl}-amino)-acetate;

Ethyl-(benzyl-{4-[2-(5-ethyl-pyridin-2-yl)-ethoxy]-benzyl}-amino)-acetate;

Ethyl-{benzyl-[4-(2-fluoro-benzyloxy)-benzyl]-amino}-acetate;

Ethyl-[benzyl-(4-{2-[2-(4-methoxy-phenyl)-5-methyl-pyrrol-1-yl]-ethoxy}-benzyl)-amino]- acetate;

Ethyl-[benzyl-(4-{2-[2-methyl-5-(5-methyl-thiophen-2-yl)-pyrrol-1-yl]-ethoxy}-benzyl)-amino]-acetate;

Ethyl-[benzyl-(4-{2-[5-methyl-2-(5-methyl-thiophen-2-yl)-oxazol-4-yl]-ethoxy}-benzyl)-amino]-acetate;

Ethyl-(benzyl-{4-[2-(2,3-dihydro-benzo[1,4]thiazin-4-yl)-ethoxy]-benzyl}-amino)-acetate;

Ethyl-(benzyl-{4-[2-(5-methyl-2-thiophen-3-yl-oxazol-4-yl)-ethoxy]-benzyl}-amino)-acetate;

Ethyl-({4-[2-(2-benzo[b]thiophen-2-yl-5-methyl-oxazol-4-yl)-ethoxy]-benzyl}-benzyl-amino)-acetate;

Ethyl-{benzyl-[4-(3-methyl-4-oxo-3,4-dihydro-quinazolin-2-ylmethoxy)-benzyl]-amino}-acetate;

Ethyl-{benzyl-[4-(2-phenoxazin-10-yl-ethoxy)-benzyl]-amino}-acetate;

Ethyl-(benzyl-{4-[2-(3,4-dihydro-2H-quinolin-1-yl)-ethoxy]-benzyl}-amino)-acetate;

Ethyl-[{4-[2-(5-ethyl-pyridin-2-yl)-ethoxy]-benzyl}-(4-methoxy-phenoxycarbonyl)-amino]-acetate;

Ethyl-((4-methoxy-phenoxycarbonyl)-{4-[2-(methyl-pyridin-2-yl-amino)-ethoxy]-benzyl}-amino)-acetate;

Ethyl-[(4-methoxy-phenoxycarbonyl)-(4-{2-[2-methyl-5-(5-methyl-thiophen-2-yl)-pyrrol-1-yl]-ethoxy}-benzyl)-amino]-acetate;

Methyl-((4-methoxy-phenoxycarbonyl)-{4-[2-(5-methyl-2-thiophen-2-yl-oxazol-4-yl)-ethoxy]-benzyl}-amino)-acetate;

Ethyl-[(4-methoxy-phenoxycarbonyl)-(4-{2-[5-methyl-2-(5-methyl-thiophen-2-yl)-oxazol-4-yl]-ethoxy}-benzyl)-amino]-acetate;

Ethyl-{(4-methoxy-phenoxycarbonyl)-[4-(3-methyl-4-oxo-3,4-dihydro-quinazolin-2-ylmethoxy)-benzyl]-amino}-acetate;

Ethyl-[[4-(2-fluoro-benzyloxy)-benzyl]-(4-methoxy-phenoxycarbonyl)-amino]-acetate;

Ethyl-[(4-methoxy-phenoxycarbonyl)-(4-{2-[2-methyl-5-(4-methylsulfanyl-phenyl)-pyrrol-1-yl]-ethoxy}-benzyl)-amino]-acetate;

Ethyl-[{4-[2-(2-furan-2-yl-5-methyl-oxazol-4-yl)-ethoxy]-benzyl}-(4-methoxy-phenoxycarbonyl)-amino]-acetate;

Ethyl-[{4-[2-(3-ethyl-4-methyl-6-oxo-2-thioxo-3,6-dihydro-2H-pyrimidin-1-yl)-ethoxy]-benzyl}-(4-methoxy-phenoxycarbonyl)-amino]-acetate;

Ethyl-((4-methoxy-phenoxycarbonyl)-{4-[2-(2,5,6-trimethyl-4-oxo-4H-thieno[2,3-d]pyrimidin-3-yl)-ethoxy]-benzyl}-amino)-acetate;

Ethyl-[{4-[2-(3,4-dihydro-2H-quinolin-1-yl)-ethoxy]-benzyl}-(4-methoxy-phenoxycarbonyl)-amino]-acetate;

Ethyl-[{3-[2-(2-furan-2-yl-5-methyl-oxazol-4-yl)-ethoxy]-benzyl}-(4-methoxy-phenoxycarbonyl)-amino]-acetate;

Ethyl-((4-methoxy-phenoxycarbonyl)-{4-[2-(methyl-pyrimidin-2-yl-amino)-ethoxy]-benzyl}-amino)-acetate;

Ethyl-[{4-[2-(2-benzo[1,3]dioxol-5-yl-5-methyl-pyrrol-1-yl)-ethoxy]-benzyl}-(4-methoxy-phenoxycarbonyl)-amino]-acetate;

Ethyl-[[4-(2-benzoimidazol-1-yl-ethoxy)-benzyl]-(4-methoxy-phenoxycarbonyl)-amino]-acetate;

Ethyl-{3-[2-(2-benzo[1,3]dioxol-5-yl-5-methyl-pyrrol-1-yl)-ethoxy]-benzyl}-(4-methoxy-phenoxycarbonyl)-amino]-acetate;

Ethyl-[[4-(2-benzoimidazol-1-yl-ethoxy)-benzyl]-(4-methoxy-phenoxycarbonyl)-amino]-acetate;

Ethyl-{(4-methoxy-phenoxycarbonyl)-[4-(1-methyl-1H-benzoimidazol-2-ylmethoxy)-benzyl]-amino}-acetate;

Ethyl-[(4-methoxy-phenoxycarbonyl)-(4-{2-[5-methyl-2-(5-methyl-furan-2-yl)-oxazol-4-yl]-ethoxy}-benzyl)-amino]-acetate;

Ethyl-[[4-(6-methoxy-1-methyl-1H-benzoimidazol-2-ylmethoxy)-benzyl]-(4-methoxy-phenoxycarbonyl)-amino]-acetate;

Ethyl-[(4-{2-[2-(5-bromo-thiophen-2-yl)-5-methyl-oxazol-4-yl]-ethoxy}-benzyl)-(4-methoxy-phenoxycarbonyl)-amino]-acetate;

Ethyl-[[4-(benzothiazol-2-ylmethoxy)-benzyl]-(4-methoxy-phenoxycarbonyl)-amino]-acetate;

Ethyl-[benzyloxycarbonyl-(4-{2-[2-methyl-5-(5-methyl-thiophen-2-yl)-pyrrol-1-yl]-ethoxy}-benzyl)-amino]-acetate;

Ethyl-{(4-methoxy-phenoxycarbonyl)-[4-(2-morpholin-4-yl-ethoxy)-benzyl]-amino}-acetate;

Ethyl-[(4-methoxy-phenoxycarbonyl)-(4-{2-[methyl-(4-nitro-phenyl)-amino]-ethoxy}-benzyl)-amino]-acetate;

Ethyl-[(4-methoxy-phenoxycarbonyl)-(3-{2-[2-methyl-5-(5-methyl-thiophen-2-yl)-pyrrol-1-yl]ethoxy}benzyl)-amino]-acetate;

Ethyl-[[4-(benzooxazol-2-ylmethoxy)-benzyl]-(4-methoxy-phenoxycarbonyl)-amino]-acetate;

Ethyl-[(4-methoxy-phenoxycarbonyl)-(3-{2-[2-methyl-5-(4-methylsulfanyl-phenyl)-pyrrol-1-yl]-ethoxy}-benzyl)-amino]-acetate;

Ethyl-((4-methoxy-phenoxycarbonyl)-{4-[2-(5-methyl-3-phenyl-isoxazol-4-yl)-ethoxy]-benzyl}-amino)-acetate;

(Benzyl-{3-[2-(3,4-dihydro-2H-quinolin-1-yl)-ethoxy]-benzyl}-amino)-acetic acid and its pharmaceutically acceptable salts;

(Benzyl-{3-[2-(4-methanesulfonyloxy-phenyl)-ethoxy]-benzyl}-amino)-acetic acid and its pharmaceutically acceptable salts;

{Benzyl-[3-(2-phenoxazin-10-yl-ethoxy)-benzyl]-amino}-acetic acid and its pharmaceutically acceptable salts;

{Benzyl-[3-(2-carbazol-9-yl-ethoxy)-benzyl]-amino}-acetic acid and its pharmaceutically acceptable salts;

(Benzyl-{3-[2-(5-ethyl-pyridin-2-yl)-ethoxy]-benzyl}-amino)-acetic acid and its pharmaceutically acceptable salts;

(Benzyl-{3-[2-(2,3-dihydro-benzo[1,4]oxazin-4-yl)-ethoxy]-benzyl}-amino)-acetic acid and its pharmaceutically acceptable salts;

(Benzyl-{3-[2-(2,3-dihydro-benzo[1,4]thiazin-4-yl)-ethoxy]-benzyl}-amino)-acetic acid and its pharmaceutically acceptable salts;

{Benzyl-[3-(2-indol-1-yl-ethoxy)-benzyl]-amino}-acetic acid and its pharmaceutically acceptable salts;

{Benzyl-[3-(3-phenothiazin-10-yl-propoxy)-benzyl]-amino}-acetic acid and its pharmaceutically acceptable salts;

{Benzyl-[3-(3-methyl-4-oxo-3,4-dihydro-quinazolin-2-ylmethoxy)-benzyl]-amino}-acetic acid and its pharmaceutically acceptable salts;

[Benzyl-(3-{2-[2-methyl-5-(4-methylsulfanyl-phenyl)-pyrrol-1-yl]-ethoxy}-benzyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

{(4-Methoxy-phenoxycarbonyl)-[4-(2-phenoxazin-10-yl-ethoxy)-benzyl]-amino}-acetic acid and its pharmaceutically acceptable salts;

{(4-Methoxy-phenoxycarbonyl)-[4-(2-phenothiazin-10-yl-ethoxy)-benzyl]-amino}-acetic acid and its pharmaceutically acceptable salts;

{(4-Methoxy-phenoxycarbonyl)-[4-(2-oxo-3-phenyl-oxazolidin-5-ylmethoxy)-benzyl]-amino}-acetic acid and its pharmaceutically acceptable salts;

[(6-Benzyloxy-naphthalen-2-ylmethyl)-(4-methoxy-phenoxycarbonyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

{(4-Methoxy-phenoxycarbonyl)-[6-(1-phenyl-pentyloxy)-naphthalen-2-ylmethyl]-amino}-acetic acid and its pharmaceutically acceptable salts;

[{4-[2-(6,7-Dihydro-4H-thieno[3,2-c]pyridin-5-yl)-ethoxy]-benzyl}-(4-methoxy-phenoxycarbonyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

[{4-[2-(2,3-Dihydro-benzo[1,4]thiazin-4-yl)-ethoxy]-benzyl}-(4-methoxy-phenoxycarbonyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

[[4-(2-Indol-1-yl-ethoxy)-benzyl]-(4-methoxy-phenoxycarbonyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

[[4-(2-Carbazol-9-yl-ethoxy)-benzyl]-(4-methoxy-phenoxycarbonyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

{(4-Methoxy-phenoxycarbonyl)-[4-(1-pyridin-2-yl-pyrrolidin-2-ylmethoxy)-benzyl]-amino}-acetic acid and its pharmaceutically acceptable salts;

[{4-[2-(2,3-Dihydro-benzo[1,4]oxazin-4-yl)-ethoxy]-benzyl}-(4-methoxy-phenoxycarbonyl)-amino]-aceticacid and its pharmaceutically acceptable salts;

(Carboxymethyl-{4-[2-(5-methyl-2-phenyl-oxazol-4-yl)-ethoxy]-benzyl}-amino)-acetic acid and its pharmaceutically acceptable salts;

(Benzyl-{4-[2-(5-methyl-2-thiophen-2-yl-oxazol-4-yl)-ethoxy]-benzyl}-amino)-acetic acid and its pharmaceutically acceptable salts;

(Benzyl-{3-[2-(5-methyl-2-thiophen-2-yl-oxazol-4-yl)-ethoxy]-benzyl}-amino)-acetic acid and its pharmaceutically acceptable salts;

[Benzyl-(4-{2-[2-methyl-5-(4-methylsulfanyl-phenyl)-pyrrol-1-yl]-ethoxy}-benzyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

(Benzyl-{4-[2-(methyl-pyridin-2-yl-amino)-ethoxy]-benzyl}-amino)-acetic acid and its pharmaceutically acceptable salts;

(Benzyl-{4-[2-(5-ethyl-pyridin-2-yl)-ethoxy]-benzyl}-amino)-acetic acid and its pharmaceutically acceptable salts;

{Benzyl-[4-(2-fluoro-benzyloxy)-benzyl]-amino}-acetic acid and its pharmaceutically acceptable salts;

[Benzyl-(4-{2-[2-(4-methoxy-phenyl)-5-methyl-pyrrol-1-yl]-ethoxy}-benzyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

[Benzyl-(4-{2-[2-methyl-5-(5-methyl-thiophen-2-yl)-pyrrol-1-yl]-ethoxy}-benzyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

[Benzyl-(4-{2-[5-methyl-2-(5-methyl-thiophen-2-yl)-oxazol-4-yl]-ethoxy}-benzyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

(Benzyl-{4-[2-(2,3-dihydro-benzo[1,4]thiazin-4-yl)-ethoxy]-benzyl}-amino)-acetic acid

(Benzyl-{4-[2-(5-methyl-2-thiophen-3-yl-oxazol-4-yl)-ethoxy]-benzyl}-amino)-acetic acid and its pharmaceutically acceptable salts;

({4-[2-(2-Benzo[b]thiophen-2-yl-5-methyl-oxazol-4-yl)-ethoxy]-benzyl}-benzyl-amino)-acetic acid and its pharmaceutically acceptable salts;

{Benzyl-[4-(3-methyl-4-oxo-3,4-dihydro-quinazolin-2-ylmethoxy)-benzyl]-amino}-acetic acid and its pharmaceutically acceptable salts;

{Benzyl-[4-(2-phenoxazin-10-yl-ethoxy)-benzyl]-amino}-acetic acid and its pharmaceutically acceptable salts;

(Benzyl-{4-[2-(3,4-dihydro-2H-quinolin-1-yl)-ethoxy]-benzyl}-amino)-acetic acid and its pharmaceutically acceptable salts;

[{4-[2-(5-Ethyl-pyridin-2-yl)-ethoxy]-benzyl}-(4-methoxy-phenoxycarbonyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

((4-Methoxy-phenoxycarbonyl)-{4-[2-(methyl-pyridin-2-yl-amino)-ethoxy]-benzyl}-amino)-acetic acid and its pharmaceutically acceptable salts;

[(4-Methoxy-phenoxycarbonyl)-(4-{2-[2-methyl-5-(5-methyl-thiophen-2-yl)-pyrrol-1-yl]-ethoxy}-benzyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

((4-Methoxy-phenoxycarbonyl)-{4-[2-(5-methyl-2-thiophen-2-yl-oxazol-4-yl)-ethoxy]-benzyl}-amino)-acetic acid and its pharmaceutically acceptable salts;

[(4-Methoxy-phenoxycarbonyl)-(4-{2-[5-methyl-2-(5-methyl-thiophen-2-yl)-oxazol-4-yl]-ethoxy}-benzyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

{(4-Methoxy-phenoxycarbonyl)-[4-(3-methyl-4-oxo-3,4-dihydro-quinazolin-2-ylmethoxy)-benzyl]-amino}-acetic acid and its pharmaceutically acceptable salts;

[[4-(2-Fluoro-benzyloxy)-benzyl]-(4-methoxy-phenoxycarbonyl)-amino]-acetic acid

[(4-Methoxy-phenoxycarbonyl)-(4-{2-[2-methyl-5-(4-methylsulfanyl-phenyl)-pyrrol-1-yl]-ethoxy}-benzyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

[{4-[2-(2-Furan-2-yl-5-methyl-oxazol-4-yl)-ethoxy]-benzyl}-(4-methoxy-phenoxycarbonyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

[{4-[2-(3-Ethyl-4-methyl-6-oxo-2-thioxo-3,6-dihydro-2H-pyrimidin-1-yl)-ethoxy]-benzyl}-(4-methoxy-phenoxycarbonyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

((4-Methoxy-phenoxycarbonyl)-{4-[2-(2,5,6-trimethyl-4-oxo-4H-thieno[2,3-d]pyrimidin-3-yl)-ethoxy]-benzyl}-amino)-acetic acid and its pharmaceutically acceptable salts;

[{4-[2-(3,4-Dihydro-2H-quinolin-1-yl)-ethoxy]-benzyl}-(4-methoxy-phenoxycarbonyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

[{3-[2-(2-Furan-2-yl-5-methyl-oxazol-4-yl)-ethoxy]-benzyl}-(4-methoxy-phenoxycarbonyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

((4-Methoxy-phenoxycarbonyl)-{4-[2-(methyl-pyrimidin-2-yl-amino)-ethoxy]-benzyl}-amino)-acetic acid and its pharmaceutically acceptable salts;

[{4-[2-(2-Benzo[1,3]dioxol-5-yl-5-methyl-pyrrol-1-yl)-ethoxy]-benzyl}-(4-methoxy-phenoxycarbonyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

[[4-(2-Benzotriazol-1-yl-ethoxy)-benzyl]-(4-methoxy-phenoxycarbonyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

[(4-Methoxy-phenoxycarbonyl)-(4-{2-[5-methyl-2-(5-methyl-furan-2-yl)-oxazol-4-yl]-ethoxy}-benzyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

[{3-[2-(2-Benzo[1,3]dioxol-5-yl-5-methyl-pyrrol-1-yl)-ethoxy]-benzyl}-(4-methoxy-phenoxycarbonyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

[[4-(2-Benzoimidazol-1-yl-ethoxy)-benzyl]-(4-methoxy-phenoxycarbonyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

{(4-Methoxy-phenoxycarbonyl)-[4-(1-methyl-1H-benzoimidazol-2-ylmethoxy)-benzyl]-amino}-acetic acid and its pharmaceutically acceptable salts;

[[4-(6-Methoxy-1-methyl-1H-benzoimidazol-2-ylmethoxy)-benzyl]-(4-methoxy-phenoxycarbonyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

[(4-{2-[2-(5-Bromo-thiophen-2-yl)-5-methyl-oxazol-4-yl]-ethoxy}-benzyl)-(4-methoxy-phenoxycarbonyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

[(4-Methoxy-phenoxycarbonyl)-(3-{2-[2-methyl-5-(4-methylsulfanyl-phenyl)-pyrrol-1-yl]-ethoxy}-benzyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

[[4-(Benzothiazol-2-ylmethoxy)-benzyl]-(4-methoxy-phenoxycarbonyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

((4-Methoxy-phenoxycarbonyl)-{4-[2-(5-methyl-3-phenyl-isoxazol-4-yl)-ethoxy]-benzyl}-amino)-acetic acid and its pharmaceutically acceptable salts;

{(4-Methoxy-phenoxycarbonyl)-[4-(2-morpholin-4-yl-ethoxy)-benzyl]-amino}-acetic acid and its pharmaceutically acceptable salts;

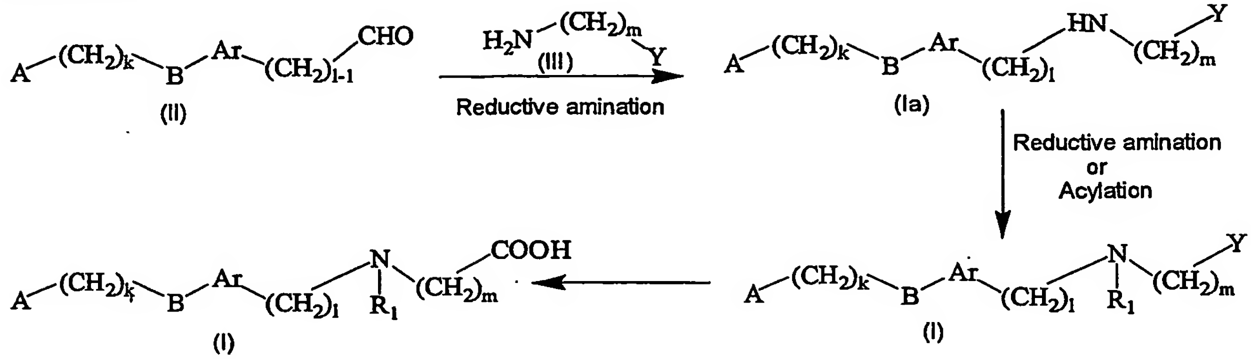
[(4-Methoxy-phenoxycarbonyl)-(4-{2-[methyl-(4-nitro-phenyl)-amino]-ethoxy}-benzyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

[(4-Methoxy-phenoxycarbonyl)-(3-{2-[2-methyl-5-(5-methyl-thiophen-2-yl)-pyrrol-1-yl]-ethoxy}-benzyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

[[4-(Benzooxazol-2-ylmethoxy)-benzyl]-(4-methoxy-phenoxycarbonyl)-amino]-acetic acid and its pharmaceutically acceptable salts;

The present invention also provides novel processes for the preparation of compounds of formula (I) as well as intermediates involved in their synthesis. The compounds of the present invention can be prepared according to the general schemes provided below:

Scheme 1:



The compounds of general formula (I) wherein all the symbols are as defined earlier may be prepared by according to the process outlined in scheme 1 above, which comprises i) reacting the aldehyde of formula (II) wherein all the symbols are as defined earlier with protected amino acids of formula (III) wherein Y denotes suitably protected carboxyl group such as an alkyl ester or amide and the like, in the presence of suitable reducing agents to obtain a compound of formula (Ia). Compound (Ia) represents compound of formula (I) where R_1=H. Suitable reducing agents like sodium borohydride, sodium triacetoxyborohydride, tetrabutyl ammonium borohydride and the like may be employed. The reaction may be carried out in solvents appropriate for the reagent used e.g. alcohols may be used with borohydrides and halogenated solvents such as 1,2-dichloroethane and the like or alcohols such as methanol, ethanol, propanol, isopropanol, butanol, *t*-butanol and the like or mixtures thereof may be used with sodium triacetoxyborohydride. Reaction temperatures may range from 0°C to reflux temperature of the solvent(s) used. Reactions may be carried out in an atmosphere of inert gases like nitrogen, argon and the like but is not critical.

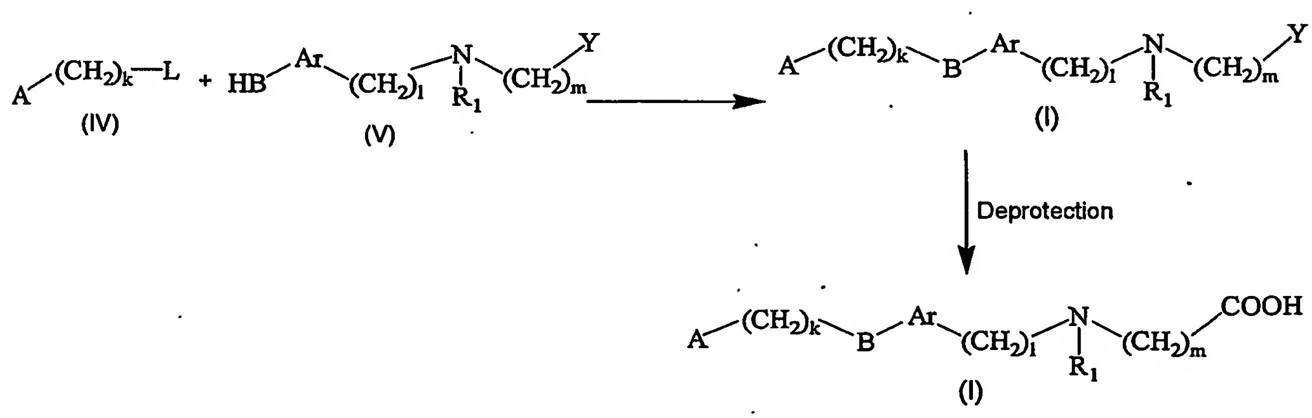
ii) compounds of general formula (Ia) wherein R_1 = H & all other symbols are as defined earlier, may be converted to compounds of general formula (I) wherein all the symbols are as defined earlier by another reductive amination with an appropriate aldehyde (e.g. to get R_1 = suitable alkyl derivative, corresponding aldehyde may be used; benzaldehyde may be used when R_1 is benzyl group) by a process similar to that described in (i) above or by acylation using appropriate acylating agents such as acyl halides (to get corresponding R_1 = acyl), anhydrides (to get corresponding R_1 = acyl), suitable carbamoyl

chloride (to get NR_1 = urea derivatives), suitable sulfonyl halides (to get R_1 = sulfonates), haloformates (to get NR_1 = carbamate) and the like. Reaction may be carried out in the presence of an inorganic base such as (aqueous) sodium(bi)carbonate, potassium(bi)carbonate, sodium or potassium hydroxide and the like or an organic base such as trialkyl amine, pyridine and the like. Solvents such as halogenated hydrocarbons (dichloromethane, dichloroethane, chloroform and the like), DMF, DMSO, ethers (diethyl ether, methyl *tert* butyl ether, tetrahydrofuran and the like) or mixtures thereof may be employed. Reaction temperatures may range from 0 ^{0}C to reflux temperature of the solvent(s) used. Reactions may be carried out in an atmosphere of inert gases like nitrogen, argon and the like but is not critical.

iii) the compound of general formula (I) (where $R_3 \neq$ -OH), and all other symbols are as defined earlier may be optionally converted to compound of general formula (I) (R_3 = -OH), by deprotecting the protected carboxyl group by using suitable deprotection methods e.g. acidic or basic hydrolysis may be employed when 'Y' is an ester. Aqueous alcohols and the like may be used as solvents. Reaction temperatures may range from 0 ^{0}C to reflux temperature of the solvent(s) used.

iv) optionally, if desired, the compounds of formula (I) are converted to their pharmaceutically acceptable salts by techniques known in the art.

Scheme 2:



Alternatively, the compounds of general formula (I) wherein all the symbols are as defined earlier & $R_3 \neq$ OH & NH_2 may be prepared by a sequence of reactions outlined in

scheme 2 above which further may be converted to compound of general formula (I) by methods similar to those described in scheme 1 which comprises;

i) reacting compounds of general formula (IV) where L represents a suitable leaving group such as halogen, mesylate, tosylate, triflate & the like, with compounds of general formula (V) to obtain the compound of general formula (I). Suitable bases like metal hydrides e.g. NaH, KH and the like, alkali metal carbonates e.g. potassium carbonate, sodium carbonate and the like, sodium hydroxide, potassium hydroxide, alkoxides such as NaOMe, NaOEt, potassium *t*-butoxide, sodium *t*-butoxide, sodium amyloxide and the like may be used. Reaction may be carried out in suitable solvents like DMF, DMSO, THF, toluene and the like or mixture thereof. Acetone may also be used with alkali metal carbonates. Reaction temperature may range from 0 ^{o}C to the reflux temperature of the solvent(s) used. Inert atmosphere may be maintained using N_2, He, or argon gas. Reaction time may range from 1 to 72 hours.

ii) converting the compound of formula (I) to a further compound of formula (I) by the process as described in scheme 1 above.

iii) optionally, if desired, the compounds of formula I are converted to their pharmaceutically acceptable salts by techniques known in the art.

It will be appreciated that in any of the above mentioned reactions any reactive group in the substrate molecule may be protected, according to conventional chemical practice. Suitable protecting groups in any of the above mentioned reactions are those used conventionally in the art. The methods of formation and removal in such protecting groups are those conventional methods appropriate to the molecule being protected. T. W. Greene and P. G. M. Wuts "Protective groups in Organic Synthesis", John Wiley & Sons, Inc, 1999, 3rd Ed., 201-245 along with references therein.

The pharmaceutically acceptable salts forming a part of this invention may be prepared by treating the compound of formula (I) with 1-6 equivalents of a base such as sodium hydride, sodium methoxide, sodium ethoxide, sodium hydroxide, potassium tert-butoxide, calcium hydroxide, calcium acetate, calcium chloride, magnesium hydroxide, magnesium chloride, magnesium alkoxide and the like. Solvents such as water, acetone, ether, THF, methanol, ethanol, t-butanol, 2-butanone, dioxane, propanol, butanol, isopropanol, di*iso*propyl ether, *tert*-butyl ether or mixtures thereof may be used. Organic bases such as

lysine, arginine, methyl benzylamine, ethanolamine, diethanolamine, tromethamine, choline, guanidine and their derivatives may be used. Acid addition salts, wherever applicable may be prepared by treatment with acids such as tartaric acid, mandelic acid, fumaric acid, malic acid, lactic acid, maleic acid, salicylic acid, citric acid, ascorbic acid, benzene sulfonic acid, p-toluene sulfonic acid, hydroxynaphthoic acid, methane sulfonic acid, acetic acid, benzoic acid, succinic acid, palmitic acid, hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid and the like in solvents such as water, alcohols, ethers, ethyl acetate, dioxane, THF, acetonitrile, DMF or a lower alkyl ketone such as acetone, or mixtures thereof.

Another aspect of the present invention comprises a pharmaceutical composition, containing at least one of the compounds of the general formula (I), their tautomeric forms, their pharmaceutically acceptable salts as an active ingredient, together with pharmaceutically employed carriers diluents and the like.

The novel compounds of the present invention can be formulated into suitable pharmaceutically acceptable compositions by combining with suitable excipients as are well known.

The novel compounds of the present invention can be formulated into suitable pharmaceutically acceptable compositions by combining with suitable excipients by techniques and processes and concentrations as are well known.

The compounds of formula (I) or pharmaceutical compositions containing them may be administered either by oral, topical or parenteral administration.

The pharmaceutical composition is provided by employing conventional techniques. Preferably the composition is in unit dosage form containing an effective amount of the active component, that is, the compounds of formula (I) according to this invention.

The quantity of active component, that is, the compounds of formula (I) according to this invention, in the pharmaceutical composition and unit dosage form thereof may be varied or adjusted widely depending upon the particular application method, the potency of the particular compound and the desired concentration. Generally, the quantity of active component will range between 0.5 % to 90 % by weight of the composition.

The compounds of general formula (I) or the compositions thereof are useful for the treatment and/or prophylaxis of disease caused by metabolic disorders such as

hyperlipidemia, insulin resistance, leptin resistance, hyperglycemia, obesity, or inflammation.

These compounds are useful for the treatment of hypercholesteremia, familial hypercholesteremia, hypertriglyceridemia, type 2 diabetes, dyslipidemia, disorders related to syndrome X such as hypertension, obesity, insulin resistance, coronary heart disease, atherosclerosis, xanthoma, stroke, peripheral vascular diseases and related disorders and diabetic complications.

The compounds of the invention may be administered to a mammal, especially, a human in need of such treatment, prevention, elimination, alleviation or amelioration of diseases mentioned above.

In another aspect of the present invention, method of treatment and/or prevention of the diseases mentioned above by treatment with compounds of the present invention are provided.

In a further aspect of the present invention, use of one or more compounds of the general formula (I) or pharmaceutically acceptable salts, for the preparation of a medicament thereof for the treatment and/or prevention of diseases mentioned in this document is provided.

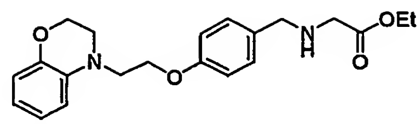
The invention is explained in detail by the examples given below, which are provided by way of illustration only and therefore should not be construed to limit the scope of the invention.

The invention is explained in detail by the examples given below, which are provided by way of illustration only and therefore should not be construed to limit the scope of the invention.

1H NMR spectral data given in the tables (vide infra) are recorded using a 300 MHz spectrometer (Bruker AVANCE-300) and reported in δ scale. Until and otherwise mentioned the solvent used for NMR is $CDCl_3$ using Tetramethyl silane as the internal standard.

<u>Preparation 1</u>

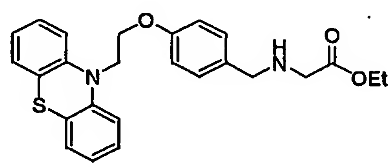
Ethyl-{4-[2-(2,3-dihydro-benzo[1,4] oxazin-4-yl)- ethoxy] benzyl amino} acetate.
(compound No.8)



To a solution of 4-[2-(2,3-dihydro-benzo [1,4] oxazin-4-yl)–ethoxy]benzaldehyde (2.3 g) and glycine ethyl ester hydrochloride (1.2 g) in methanol (40 mL) was added triethyl amine (1.3 mL) at 30 ^{0}C and the reaction mixture was cooled in an ice bath. To this was added sodium borohydride (370 mg) and stirred for one hour at 30 ^{0}C. The solvent was evaporated under reduced pressure and the residue was extracted with ethyl acetate (3X50 mL). The combined organic extract was washed with water (100 mL), brine solution (75 mL), dried over sodium sulphate and evaporated under reduced pressure. The crude product was flash chromatographed over silica gel using 25 – 40 % ethyl acetate in petroleum ether as an eluent to yield 1.35 g of pure product.

Preparation 2

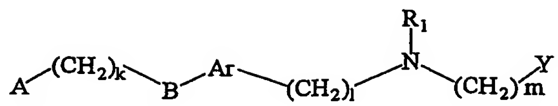
Ethyl-[4-(2-phenothiazin-10-yl-ethoxy)-benzylamino]-acetate.
(compound No.2)

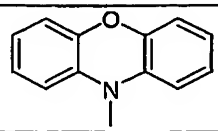
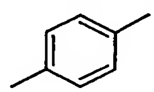
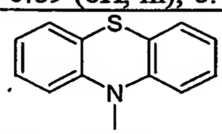
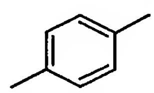
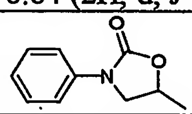
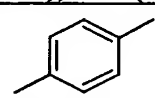
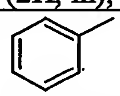
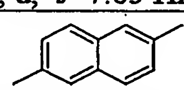
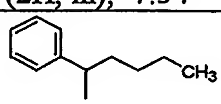
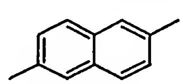
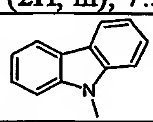
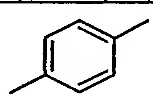


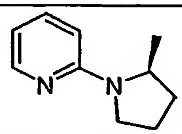
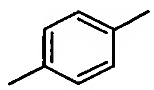
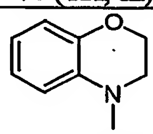
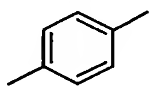
To a solution of 4-(2-phenothiazin-10-yl-ethoxy)-benzaldehyde (1.4 g) and glycine ethyl ester hydrochloride (0.59 g) in ethanol (30 mL) was added triethyl amine (0.64 mL) and the reaction mixture was stirred at 30 ^{0}C for 17 hours. The reaction mixture was cooled in an ice-bath and sodium borohydride (176 mg) was added to it in portions. Stirring was continued for 15 hours at 30 ^{0}C. The solvent was evaporated under reduced pressure and the residue was dissolved in chloroform (150 mL), washed with water (100 mL), dried over calcium chloride and evaporated under reduced pressure to yield the product (2.0 g).

The following compounds in table 1 were prepared following the procedure similar to that described for preparation 1-2.

Table 1:



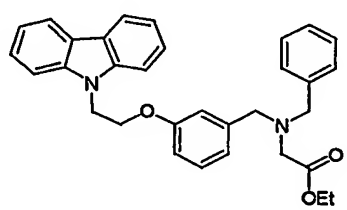
<table>
<tr><th>S.No</th><th>A</th><th>Ar</th><th>R_1</th><th>Y</th><th>B</th><th>k</th><th>l</th><th>m</th><th>Mol. Wt.</th><th>% Yield</th></tr>
<tr><td rowspan="2">1.</td><td></td><td></td><td>H</td><td>COOEt</td><td>O</td><td>2</td><td>1</td><td>1</td><td>418</td><td>71</td></tr>
<tr><td colspan="10">^{1}H: 1.27 (3H, t, J=7.14 Hz), 3.38 (2H, s), 3.73 (2H,s), 3.96 (2H, t, J=6.6 Hz), 4.2 (4H, m), 6.61 - 6.69 (6H, m), 6.76 - 6.87 (4H, m), 7.22 (2H, d, J=9.14 Hz).</td></tr>
<tr><td rowspan="2">2.</td><td></td><td></td><td>H</td><td>COOEt</td><td>O</td><td>2</td><td>1</td><td>1</td><td>434</td><td>73</td></tr>
<tr><td colspan="10">^{1}H: 1.26 (3H, t, J=7.13 Hz), 3.37 (2H, s), 3.72 (2H, s), 3.96 (2H, q, J=7.13 Hz), 4.30 (4H, s), 6.84 (2H, d, J=8.6 Hz), 6.9 (4H, d, J=7.8 Hz), 7.13 (4H, d, J=7.58 Hz), 7.25 (2H,d, J=8.58 Hz).</td></tr>
<tr><td rowspan="2">3.</td><td></td><td></td><td>H</td><td>COOMe</td><td>O</td><td>1</td><td>1</td><td>1</td><td>370</td><td>60</td></tr>
<tr><td colspan="10">^{1}H: 3.4 (2H, t, J=5.6 Hz), 3.72 (3H, s), 3.74 (2H, s), 4.07 (1H, dd, J=8.9&6.0 Hz), 4.20 - 4.25 (3H, m), 4.98 (1H, m), 6.85 (2H, d, J=8.6 Hz), 7.15 (1H, t, J=7.3 Hz), 7.26 (2H, m), 7.36 - 7.41 (2H, m), 7.56 (2H, d, J=7.83 Hz).</td></tr>
<tr><td rowspan="2">4.</td><td></td><td></td><td>H</td><td>COOEt</td><td>O</td><td>1</td><td>1</td><td>1</td><td>349</td><td>25</td></tr>
<tr><td colspan="10">^{1}H: 1.25 (3H, t, J=7.14 Hz), 3.44 (2H, s), 3.9 (2H, s), 4.2 (2H, q, J=7.14 Hz), 5.18 (2H, s), 7.2 (2H, m), 7.34 - 7.44 (4H, m), 7.48 (2H, d, J=7.1 Hz), 7.69-7.74 (3H, m).</td></tr>
<tr><td rowspan="2">5.</td><td></td><td></td><td>H</td><td>COOEt</td><td>O</td><td>0</td><td>1</td><td>1</td><td>405</td><td>52</td></tr>
<tr><td colspan="10">^{1}H: 0.9 (3H, t, J=7.1 Hz), 1.25 (3H, t, J=7.1 Hz), 1.4 (4H, complex), 1.8 (1H, m), 2.0 (1H, m), 3.39 (2H, s), 3.88 (2H, s), 4.18 (2H, q, J=7.14 Hz), 5.2 (1H, m), 6.98 (1H, d, J=2.22 Hz), 7.2 (2H, m), 7.3 (3H, m), 7.4 (2H, d, J=7.08 Hz), 7.5 (1H, J=8.43 Hz), 7.64 (2H, t, J=7.58 Hz).</td></tr>
<tr><td rowspan="2">6.</td><td></td><td></td><td>H</td><td>COOEt</td><td>O</td><td>2</td><td>1</td><td>1</td><td>402</td><td>59</td></tr>
<tr><td colspan="10">^{1}H: 1.2 (3H, t, J=7.1 Hz), 3.3 (2H, s), 3.7 (2H, s), 4.2 (2H, q, J_1=J_2=7.1 Hz), 4.3 (2H, t, J=6.0 Hz), 4.7 (2H, t, J=6.1 Hz), 6.7 (2H, d, J=8.6 Hz), 7.1 (2H, d, J=8.6 Hz), 7.2 (2H, m), 7.4-7.5 (4H, m), 8.1 (2H, d, J=7.8 Hz).</td></tr>
</table>

7.			H	COOEt	O	1	1	1	369	64
	^{1}H: 1.2 (3H, t, J=7.1 Hz), 2.0 (2H, m), 2.2 (2H, m), 3.3 (1H, m), 3.4 (2H, s), 3.5 (1H, t, J=8.7 Hz), 3.7 (2H, s), 3.8 (1H, t, J=8.7 Hz), 4.1 (2H, q, J_1 =J_2=7.1 Hz), 4.2 (1H, dd, J=9.1 & 3.2 Hz), 4.4 (1H, m), 6.4 (1H, d, J=8.5 Hz), 6.5 (1H, m), 6.9 (2H, d, J=8.6 Hz), 7.2 (2H, d, J=8.55 Hz), 7.4 (1H, m), 8.1 (1H, dd, J=4.9 & 1.1 Hz).									
8.			H	COOEt	O	2	1	1	370	30
	^{1}H: 1.27 (3H, t, J=5.95 Hz), 3.38 (2H, s), 3.51 (2H, t, J=4.41 Hz), 3.69 (2H, t, J=5.7 Hz), 3.72 (2H, s), 4.14-4.24 (6H, complex), 6.61 (1H, m), 6.68 (1H, dd, J=6.84& 8.14 Hz), 6.77-6.85 (4H, complex), 7.24 (2H, t, J=7.05 Hz).									

Preparation 3

Ethyl-{benzyl-[3-(2-carbazol-9-yl-ethoxy)-benzyl]-amino}-acetate.

(compound No.13)

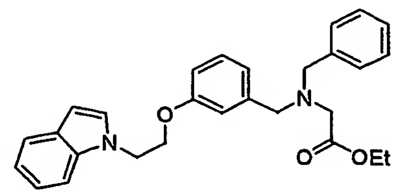


To a solution of ethyl-[3-(2-carbazol-9-yl-ethoxy)-benzyl]-amino}-acetate (compound No.6) (1.5 g) and benzaldehyde (0.4 mL) in dichloromethane (20 mL) was added sodium triacetoxy borohydride (1.0 g) and the reaction mixture was stirred at 30 ^{0}C for 36 hours. The reaction mixture was diluted with dichloromethane (75 mL) and washed with water (2X100 mL). The organic extract was dried over calcium chloride and evaporated under reduced pressure. The crude product was chromatographed (flash) over silica gel using 10 % ethyl acetate in petroleum ether as an eluent to yield 0.8 g of pure product.

Preparation 4

Ethyl-{benzyl-[3-(2-indol-1-yl-ethoxy)-benzyl]-amino}-acetate.

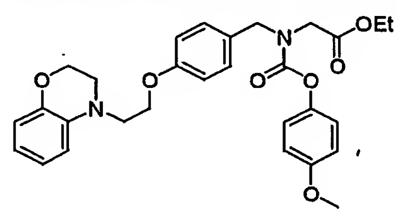
(compound No.17)



A mixture of 2-(indole-1-yl)-ethyl methanesulfonate (1.0 g), ethyl-{benzyl-[3-hydroxy benzyl]-amino}-acetate (1.25 g), potassium carbonate (1.5 g) and tetrabutylammonium bromide (10 mg) in dimethyl formamide was stirred at 60 ^{0}C for 17 hours. The reaction mixture was cooled to 30 ^{0}C and poured in to ice cold water (150 mL) and extracted with diethyl ether (3X50 mL). The combined organic extract was washed with water (100 mL), brine solution (100 mL), dried over sodium sulphate and evaporated under reduced pressure. The crude product was (flash) chromatographed over silica gel using 10 % ethyl acetate in petroleum ether as an eluent to yield 480 mg of pure product.

Preparation 5

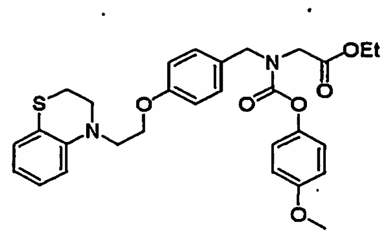
Ethyl-[{4-[2-(2,3-dihydro-benzo[1,4]oxazin-4-yl)-ethoxy]-benzyl}(4methoxyphenoxycarbonyl)-amino]-acetate. (compound No.32)



To an ice cold solution of ethyl-{4-[2-(2,3-dihydro-benzo[1,4] oxazin-4-yl)-ethoxy] benzyl amino} acetate (compound No.8) (0.9 g), and 4-methoxyphenyl chloroformate (0.5 g) in dichloromethane (5 mL) was added pyridine (0.25 mL) and the reaction mixture was stirred at ca. 0°C for 30 minutes. The reaction mixture was diluted with dichloromethane (50 mL), washed with water (25 mL), 1.0 N HCl (25 mL) followed by water (25 mL), dried over calcium chloride and evaporated under reduced pressure. The crude product was chromatographed over silica gel using 10-20 % ethyl acetate in petroleum ether as an eluent to yield 0.5 g pure product.

Preparation 6

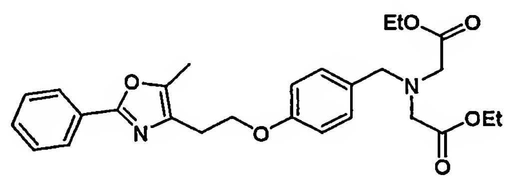
Ethyl-[{4-[2-(2,3-dihydro-benzo[1,4]thiazin-4-yl)-ethoxy]-benzyl}-(4-methoxy-phenoxycarbonyl)-amino]-acetate.(compound No.28)



A mixture of 2-{(2,3-dihydro-benzo[1,4]thiazin-4-yl)-ethyl}methane sulfonate (1 g) , ethyl-[{4-hydroxy benzyl}-(4-methoxy-phenoxycarbonyl)-amino]-acetate (1.4 g) and potassium carbonate (1.0 g) in 10 mL of dimethyl formamide was stirred at 70 ^{0}C after adding 30 mg of tetrabutyl ammonium bromide. The reaction mixture was cooled to 30 ^{0}C and water (150 mL) was added. This was extracted with ethyl acetate (3X50 mL). The combined organic extract was washed with water (2X100 mL), brine solution (100 mL), dried over sodium sulphate and evaporated under reduced pressure. The crude product was chromatographed over silica gel using 10 – 20 % ethyl acetate in petroleum ether as an eluent to yield 1.7 g of pure product.

Preparation 7

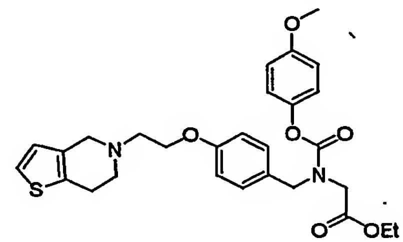
Ethyl-(ethoxycarbonylmethyl-{4-[2-(5-methyl-2-phenyl-oxazol-4-yl)-ethoxy]-benzyl}-amino)-acetate. (Compound No.33)



To a stirred and ice cold suspension of 60 % sodium hydride (183 mg) in dry THF (5 mL) was added a solution of ethyl-{4-[2-(5-methyl-2-phenyl-oxazol-4-yl)-ethoxy]-benzylamino}-acetate (1.0 g) in dry THF (5 mL) and the reaction mixture was stirred at 30 ^{0}C for 3 hours. The reaction mixture was again cooled in an ice-bath and to it was added ethyl bromoacetate (0.3 mL) and the reaction mixture was stirred at 30 ^{0}C for 18 hours. The reaction mixture was poured into ice cold water (100 mL) and extracted with ethyl acetate (3X50 mL). The combined organic extract was washed with water (50 mL), brine solution (50 mL), dried over sodium sulphate and evaporated under reduced pressure. The crude product was flash chromatographed over silica gel using 5 % ethyl acetate in petroleum ether as an eluent to obtain 1.1 g of pure product.

Preparation 8

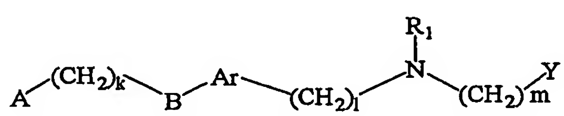
Ethyl-[{4-[2-(6,7-dihydro-4H-thieno[3,2-c]pyridin-5-yl)-ethoxy]-benzyl}-(4-methoxy-phenoxycarbonyl)-amino]-acetate (compound.No.27).

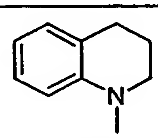
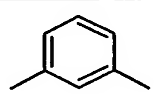
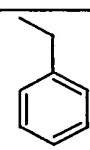


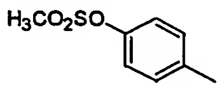
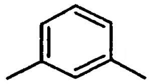
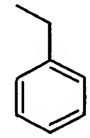
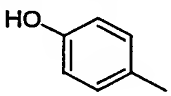
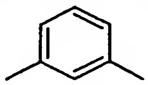
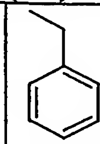
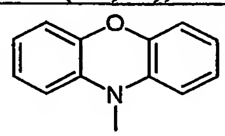
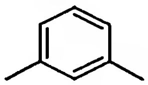
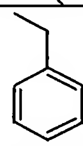
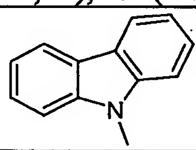
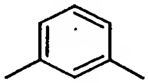
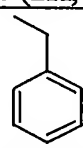
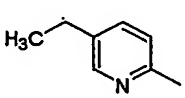
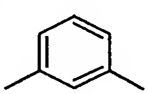
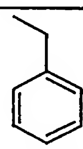
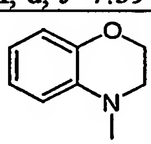
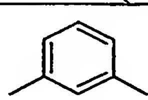
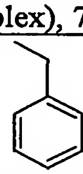
To an ice cold and stirred mixture of Ph_3P (0.95 g) and diisopropyl azodicarboxylate (0.71 mL) in dry THF (5 mL) was added a solution of 2-(6,7-dihydro-4H-thieno[3,2-c]pyridin-5-yl)-ethanol (0.5 g) in THF, followed by a solution of ethyl-[(4-hydroxy-benzyl)-(4-methoxy-phenoxycarbonyl)-amino]-acetate (1.0 g) in THF and the reaction mixture was stirred at 30 ^{0}C for 1.5 hours. The reaction mixture was poured in to ice cold water (50 mL) and extracted with ethyl acetate (3 X50 mL). The combined organic extract was washed with water (50 mL), brine solution (50 mL), dried over sodium sulphate and evaporated under reduced pressure to yield 1.0 g crude product which was hydrolysed as such without purification.

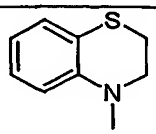
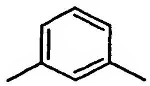
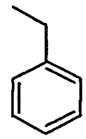
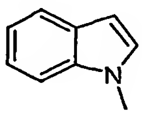
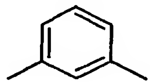
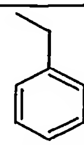
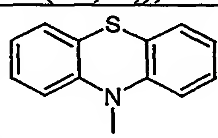
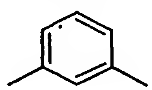
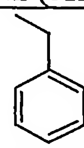
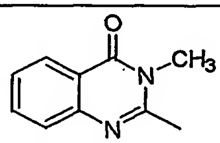
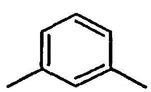
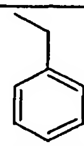
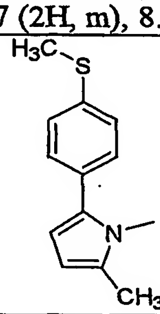
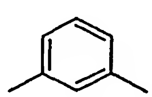
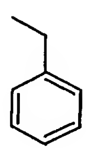
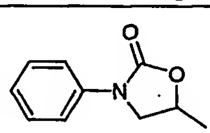
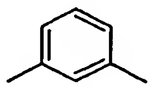
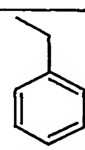
In like manner compounds in table 2 were prepared by a procedure similar to that described in preparation 3-8.

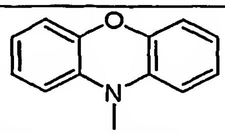
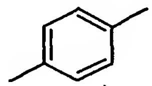
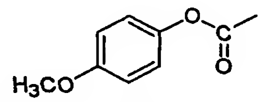
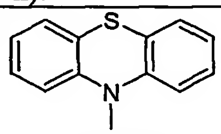
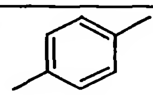
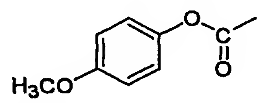
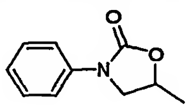
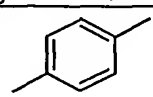
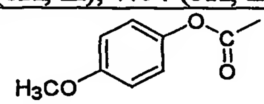
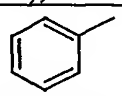
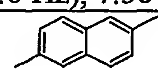
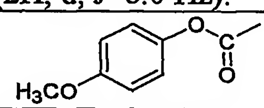
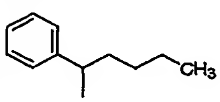
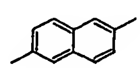
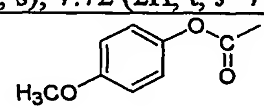
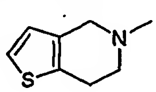
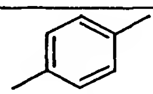
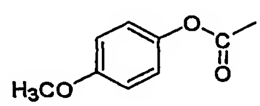
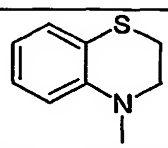
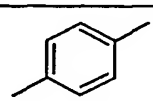
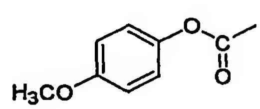
Table 2:

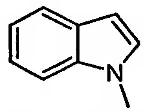
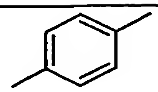
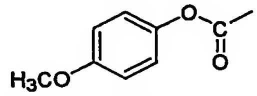
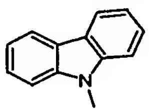
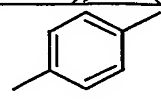
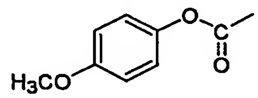
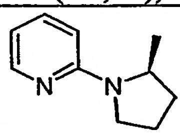
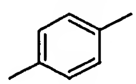
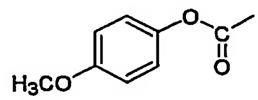
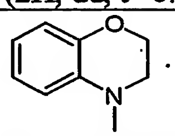
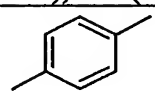
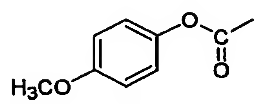
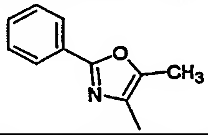
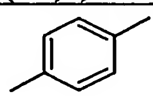
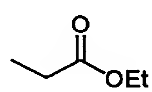
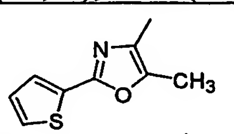
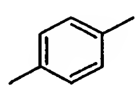
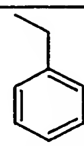
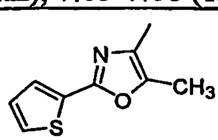
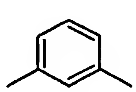
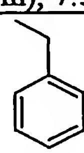


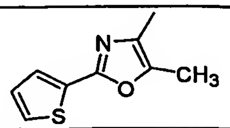
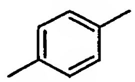
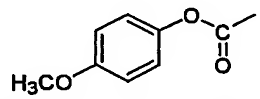
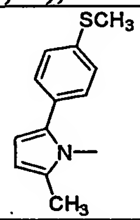
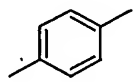
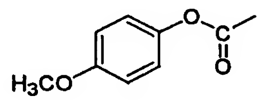
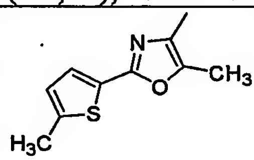
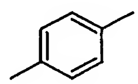
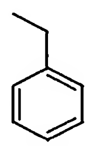
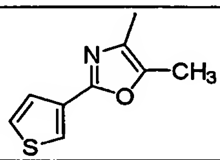
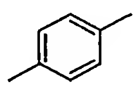
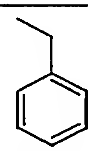
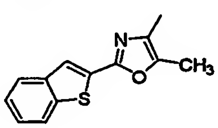
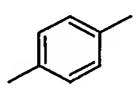
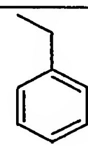
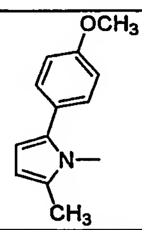
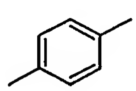
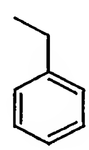
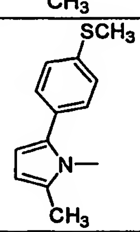
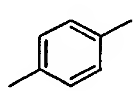
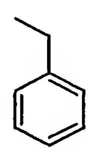
S. No	A	Ar	R1	Y	B	k	l	m	Mol. Wt.	% Yield
9.				COOEt	O	2	1	1	458	31
	^{1}H: 1.25 (3H, t, J=6.05 Hz), 1.95 (2H, m), 2.75 (2H, t, J=6.27 Hz), 3.29 (2H, s), 3.43 (2H, t, J=5.61 Hz), 3.69 (2H, t, J=6.54 Hz), 3.77 (2H, s), 3.79 (2H, s), 4.14 (4H, m), 6.61 (2H, m), 6.76 (1H, m), 6.94 (3H, m), 7.0 (1H, t, J=7.5 Hz), 7.2 – 7.4 (6H, complex).									

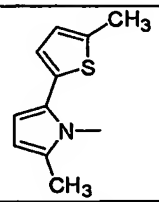
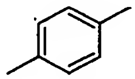
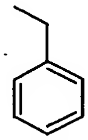
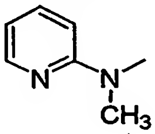
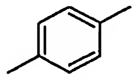
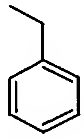
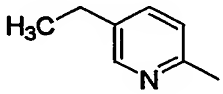
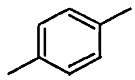
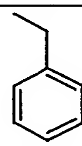
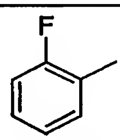
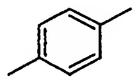
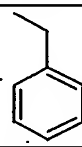
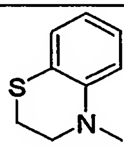
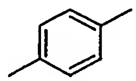
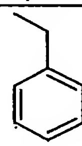
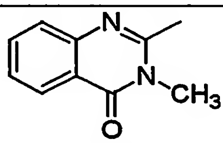
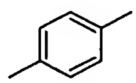
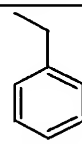
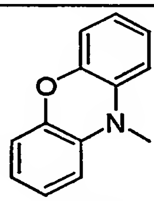
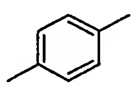
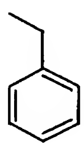
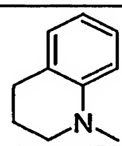
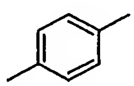
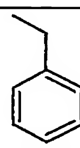
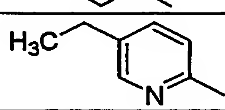
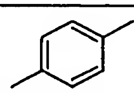
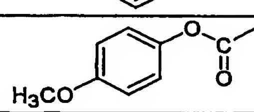
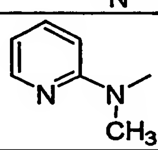
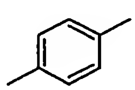
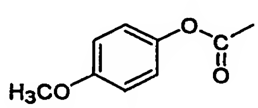
10.				COOEt	O	2	1	1	497	95
	^{1}H: 1.2 (3H, t, J=7.6 Hz), 3.0 (2H, t, J=6.7 Hz), 3.1 (3H,s), 3.2 (2H, s), 3.79 (2H, s), 3.83 (2H, s), 4.2 (4H, m), 6.9 (3H, m), 7.2 (4H, m), 7.6 (6H, m).									
11.				COOEt	O	2	1	1	419	49
	^{1}H: 1.25 (3H, t, J= 3.55 Hz), 3.0 (2H, t, J=7.01 Hz), 3.28 (2H, s), 3.77 (2H, s), 3.79 (2H, s), 4.13 (4H, m), 6.9 (3H, m), 7.2 (4H, m), 7.6 (6H,m).									
12.				COOEt	O	2	1	1	508	46
	^{1}H: 1.24 (3H, t, J=6.9 Hz), 3.2 (2H, s), 3.77 (2H, s), 3.79 (2H, s), 3.97 (2H, t, J=6.6 Hz), 4.17 (4H, m), 6.6 (6H, m), 6.78 (3H, m), 6.98 (2H, m), 7.2 – 7.3 (6H, complex).									
13.				COOEt	O	2	1	1	492	43
	^{1}H: 1.23 (3H, t, J=7.14 Hz), 3.25 (2H, s), 3.73 (2H, s), 3.76 (2H, s), 4.11 (2H, q, J=7.2 Hz), 4.36 (2H, t, J=6.5 Hz), 4.72 (2H, t, J=6.01 Hz), 6.7(1H, d, J=8.1& 2.16 Hz), 6.8 (1H, s), 6.92 (2H, m), 7.17 – 7.5 (5H, complex), 7.48 (6H, m), 8.1 (2H, d, J= 7.74 Hz).									
14.				COOEt	O	2	1	1	432	88
	^{1}H: 1.24 (6H, t), 2.62 (2H, q, J=7.6 Hz), 3.25 (2H, t, J=6.7 Hz), 3.27 (2H, s), 3.76 (2H, s), 3.79 (2H, s), 4.1 (2H, q, J=7.12 Hz), 4.34 (2H, t, J=6.7 Hz), 6.77 (1H, dd, J=9.4 & 2.1 Hz), 6.94 (2H, d, J=7.59 Hz), 7.2 – 7.4 (7H, complex), 7.46 (1H, dd, J= 2.16& 7.89 Hz), 8.4 (1H, s).									
15.				COOEt	O	2	1	1	460	79
	^{1}H: 1.2 (3H, t, J=7.14 Hz), 3.27 (2H, s), 3.5 (2H, t, J=4.4 Hz), 3.7 (2H, t, J=5.7 Hz), 3.77 (2H, s), 3.79 (2H, s), 4.1-4.18 (4H, m), 4.2 (2H, t, J=4.4 Hz), 6.6 (1H, m), 6.7 (1H, m), 6.8 (3H, m), 6.9 (2H, d, J=7.89 Hz), 7.2-7.38 (6H, m).									

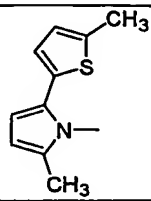
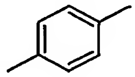
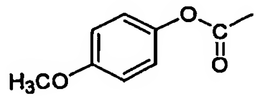
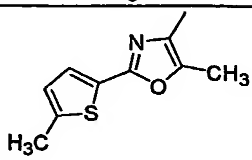
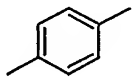
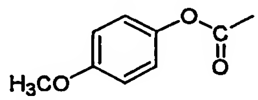
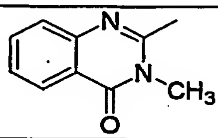
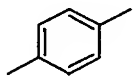
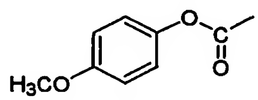
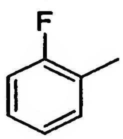
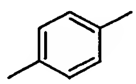
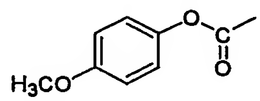
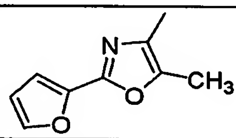
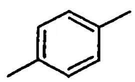
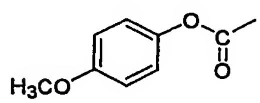
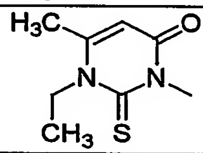
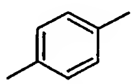
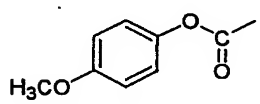
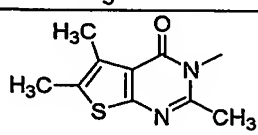
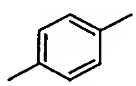
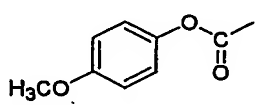
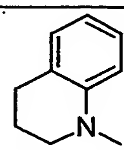
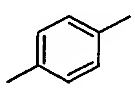
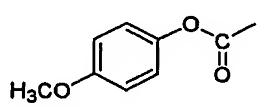
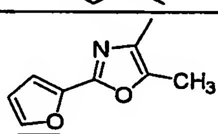
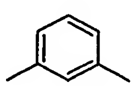
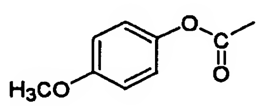
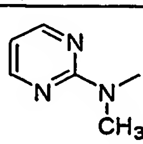
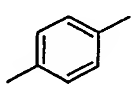
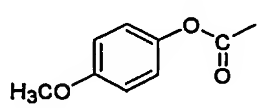
16.				COOEt	O	2	1	1	467	88
	^{1}H: 1.2 (3H, t, J= 7.13 Hz), 3.0 (2H, m), 3.28 (2H, s), 3.7-3.8 (8H, m), 4.1 (4H, m), 6.6 (1H, t, J=7.4 Hz), 6.7 (2H, m), 6.9 (2H, d, J=7.3 Hz), 7.0 (2H, dd, J=7.6&1.4 Hz), 7.18 - 7.38 (6H, m).									
17.				COOEt	O	2	1	1	442	54
	^{1}H: 1.2 (3H, t, J=7.1 Hz), 3.26 (2H, s), 3.74 (2H, s), 3.77 (2H, s), 4.1 (2H, q, J=7.1 Hz), 4.3 (2H, t, J=5.64 Hz), 4.5 (2H, t, J=5.64 Hz), 6.5 (1H, d, J=3 Hz), 6.7 (1H, dd, J=2.1& 8.1 Hz), 7.1 (2H, m,), 7.0-7.23 (5H, m), 7.29-7.42 (5H, m), 7.6 (1H, d,J=8.16 Hz).									
18.				COOEt	O	3	1	1	538	100
	^{1}H: 1.2 (3H, t, J=7.1 Hz), 2.27 (2H, m), 3.27 (2H, s), 3.75 (2H, s), 3.79 (2H, s), 4.07-4.17 (6H, m), 675 (1H, m), 6.88-6.95 (6H, m), 7.12-7.17 (5H, m), 7.22 (1H, d, J=7.78 Hz), 7.30 (2H, t, J=7.1 Hz), 7.38 (2H, d, J=7.2 Hz).									
19.				COOEt	O	1	1	1	471	56
	^{1}H: 1.2 (3H, t, J=7.1 Hz), 3.2 (2H, s), 3.74 (3H, s), 3.79 (4H, s), 4.1 (2H, q, J=7.0 Hz), 5.18 (2H, s), 6.9 (1H, dd), 7.0 (1H, d, J=7.5 Hz), 7.1 (1H, s), 7.2 - 7.3 (6H, complex), 7.5 (1H, t), 7.7 (2H, m), 8.2 (1H, d, J=7.6 Hz).									
20.				COOEt	O	2	1	1	528	50
21.				COOEt	O	1	1	1	474	85
	^{1}H: 1.2 (3H, t, J=7.1 Hz), 3.3 (2H, s), 3.77 (2H, s), 3.79 (2H, s), 4.0-4.2 (6H, m), 4.9 (1H, m), 6.8 (1H, m), 7.0 (2H, m), 7.1-7.4 (9H, complex), 7.5 (2H, d, J=8.5 Hz).									

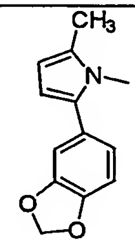
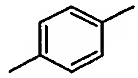
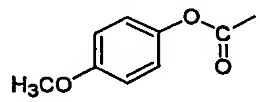
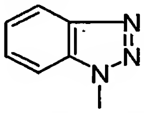
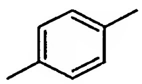
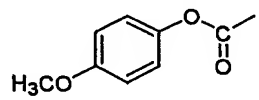
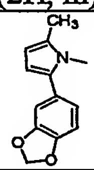
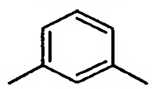
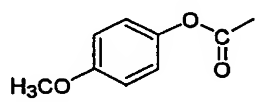
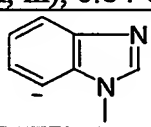
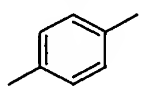
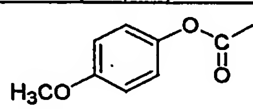
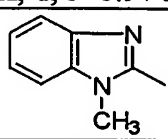
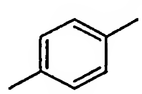
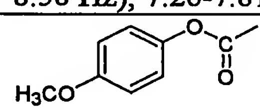
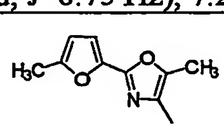
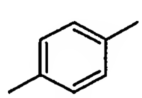
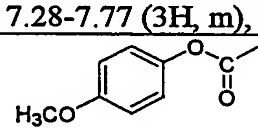
22.				COOEt	O	2	1	1	568	100
	^{1}H: 1.25 (3H, t, J=7.0 Hz), 3.72 (3H, s), 3.98 (4H, m), 4.19 (2H, m), 4.56 (1H, s), 4.66 (1H, s), 4.74 (2H, m), 6.61- 6.67 (6H, m), 6.77-6.92 (6H, m), 7.04 (2H, t, J=8.8 Hz), 7.16-7.22 (2H, m).									
23.				COOEt	O	2	1	1	584	89
	^{1}H: 1.25 (3H, t, J=7.1 Hz), 3.80 (3H, s), 4.0 (2H, m), 4.19 (2H, q, J=7.1 Hz), 4.31 (4H, s), 4.55 (1H, s), 4.66 (1H, s), 6.85- 6.96 (8H, m), 7.04 (3H, m), 7.16 (4H, d, J=7.46 Hz), 7.2 (1H, m).									
24.				COOMe	O	1	1	1	520	94
	^{1}H: 3.79 (3H, s), 3.80 (3H, s), 4.0 (2H, d, J=3.42 Hz), 4.07 (1H, m), 4.17-4.24 (3H, m), 4.57 (1H, s),4.67 (1H, s), 5.0 (1H, m), 6.85-6.92 (5H, m), 7.04 (2H, t, J=8.8 Hz), 7.13-7.19 (2H, m), 7.40 (2H, t, J=8.0 Hz), 7.56 (2H, d, J=8.0 Hz).									
25.				COOEt	O	1	1	1	499	69
	^{1}H: 1.25 (3H, t, J=7.1 Hz), 3.79 (3H, s), 4.03 (2H, s), 4.15 (2H, q, J=7.1 Hz), 4.76 (1H, s), 4.87 (1H, s), 5.18 (2H, s), 6.9 (2H, d, J=8.76 Hz), 7.07 (2H, m), 7.22 (2H, m), 7.32-7.43 (4H, m), 7.5 (2H, d, J=7.13 Hz), 7.66 (1H, s), 7.72 (2H, t, J=7.36 Hz).									
26.				COOMe	O	0	1	1	541	60
	^{1}H: 0.9 (3H, t, J=7.1 Hz), 1.36 (4H, m), 1.88 (1H, m), 2.05 (1H, m), 3.7 (3H, s), 3.79 (3H, s), 4.0 (2H, s), 4.71 (1H, s), 4.8 (1H, s), 5.2 (H, t, J=6.3 Hz), 6.8 (2H, d, J=8.3 Hz), 6.99-7.08 (3H, m), 7.18-7.23 (2H, m), 7.32 (3H, t, J=7.36 Hz), 7.4 (2H, d, J=8.05 Hz), 7.57 (2H, m), 7.68 (1H, d, J=8.9 Hz).									
27.				COOEt	O	2	1	1	524	87
28.				COOEt	O	2	1	1	536	90
	^{1}H: 1.25 (3H, t, J=7.1 Hz), 3.0 (2H, t, J=5.0 Hz), 3.74 (4H, m), 3.79 (3H, s), 3.98 (2H, m), 4.17 (4H, m), 4.56 (1H, s),4.67 (1H, s), 6.62 (1H, t, J=7.33 Hz), 6.72 (1H, d, J=8.16 Hz), 6.87 (4H, m), 6.96-7.07 (4H, m) 7.21 (2H, m).									

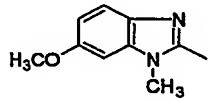
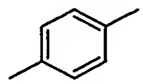
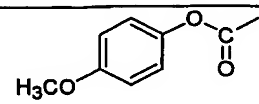
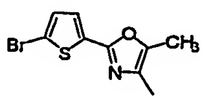
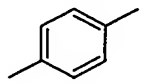
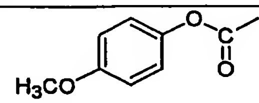
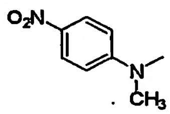
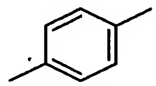
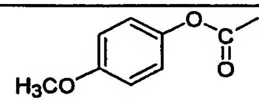
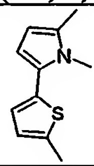
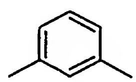
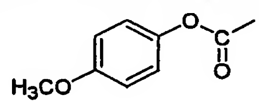
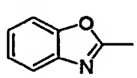
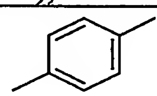
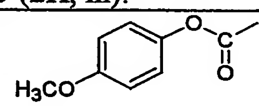
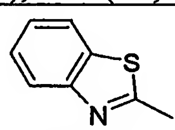
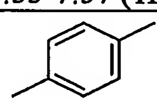
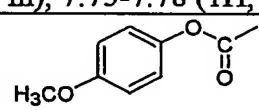
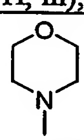
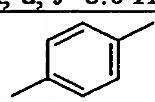
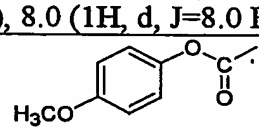
29.				COOEt	O	2	1	1	502	73
	^{1}H: 1.2 (3H, t, J=7.1 Hz), 3.78 (3H, s), 3.96 (2H, s), 4.1 (2H, m), 4.3 (2H, m), 4.5 (3H, m), 4.6 (1H, s), 6.5 (1H, d, J=3.09 Hz), 6.8-6.9 (4H, m), 7.0 (2H, m), 7.1(1H, t, J=7.44 Hz), 7.2 (4H, m), 7.4 (1H, d, J=8.32 Hz), 7.6 (1H, d, J=7.8 Hz).									
30.				COOEt	O	2	1	1	552	97
	^{1}H: 1.2 (3H, t, J=7.1 Hz), 3.75 (2H, m), 3.79 (3H, s), 4.1-4.2 (2H, m), 4.3 (2H, m), 4.5 (1H, s), 4.6 (1H, s), 4.7 (2H, m), 6.7 (2H, m), 6.8-6.9 (3H, m), 7.0 (2H, m), 7.1 (2H, m), 7.2 (1H, m), 7.5 (4H, m), 8.1 (2H, d, J=7.75 Hz).									
31.				COOEt	O	1	1	1	519	81
	^{1}H: 1.20-1.28 (3H, t, J=7.1 Hz), 2.0 (2H, m), 2.2 (2H, m), 3.3 (1H, m), 3.5 (1H, m), 3.8 (3H, s), 3.8 (1H, m), 3.98 (2H, d, J=1.9 Hz), 4.17 (2H, q, J=7.14 Hz), 4.26 (1H, m), 4.5 (1H, m), 4.55 (1H, s), 4.66 (1H, s), 6.4 (1H, d, J=8.5 Hz), 6.5 (1H, m), 6.8 (2H, m), 6.9-7.4 (4H, m), 7.2 (2H, dd, J=8.7 & 2.5 Hz), 7.4 (1H, m), 8.1(1H, m).									
32.				COOEt	O	2	1	1	520	80
	^{1}H: 1.25 (3H, t, J=7.1 Hz), 3.51 (2H, t, J=4.4 Hz), 3.70 (2H, m), 3.79 (3H, s), 4.0 (2H, m), 4.15-4.2 (6H, m), 4.56 (1H, s), 4.66 (1H, s), 6.62 (1H, m), 6.7 (1H, d, J=8.01 Hz), 6.79 (1H, m), 6.8 (5H, m), 7.0 (2H, t, J=9.54 Hz), 7.2 (2H, m).									
33.				COOEt	O	2	1	1	480	90
	^{1}H: 1.25 (6H, t, J=7.1 Hz), 2.37 (3H, s), 2.97 (2H, t, J=6.6 Hz), 3.51 (4H, s), 3.82 (2H, s), 4.1 (4H, q, J=7.1 Hz), 4.23 (2H, t, J=6.6 Hz), 6.8 (2H, d, J=8.5 Hz), 7.2 (2H, d, J=8.5 Hz), 7.35 (3H, m), 7.98 (2H, d, J=7.8 Hz).									
34.				COOEt	O	2	1	1	490	60
	^{1}H: 1.25 (3H, t, J=7.12 Hz), 2.34 (3H, s), 2.94 (2H, t, J=6.58 Hz), 3.24 (2H, s), 3.72 (2H, s), 3.77 (2H, s), 4.10-4.17 (2H, q, J=7.16 Hz), 4.2 (2H, t, J=6.61 Hz), 6.82-6.85 (2H, d, J=8.52 Hz), 7.05-7.08 (1H, m), 7.20-7.37 (8H, m), 7.56-7.58 (1H, m).									
35.				COOEt	O	2	1	1	490	60

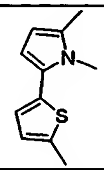
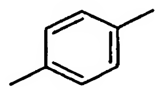
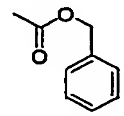
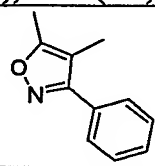
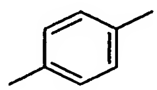
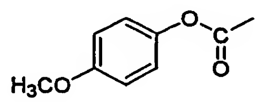
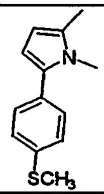
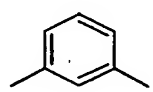
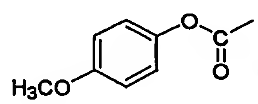
36.				COOEt	O	2	1	1	550	44
	[1]H: 1.25 (3H, t, J=7.11 Hz), 2.36 (3H, s), 2.95 (2H, t, J=6.48 Hz) 3.79 (3H, s), 3.97 (2H, s), 4.14-4.24 (4H, m), 4.55 (1H, s), 4.66 (1H, s), 6.85-6.90 (4H, m), 7.01-7.09(3H, m), 7.20-7.22 (2H, m), 7.35 (1H, m), 7.57 (1H, m).									
37.				COOEt	O	2	1	1	588	56
	[1]H: 1.27 (3H, t, J=7.25 Hz), 2.37 (3H, s), 2.51 (3H, s), 3.79 (3H, s), 3.92-3.97 (4H, m), 4.17-4.19 (2H, m), 4.28 (2H, t, J=6.4 Hz), 4.53 (1H, s), 4.64 (1H, s), 5.97 (1H, d, J=3.21 Hz), 6.10 (1H, d, J=3.36 Hz), 6.63-6.68 (2H, m), 6.88 (2H, d, J=8.85 Hz), 7.01-7.06 (2H, m), 7.15-7.18 (2H, m), 7.289-7.34(4H, m).									
38.				COOEt	O	2	1	1	504	30
39.				COOEt	O	2	1	1	490	30
40.				COOEt	O	2	1	1	540	25
41.				COOEt	O	2	1	1	512	96
42.				COOEt	O	2	1	1	528	28

43.				COOEt	O	2	1	1	502	10
44.				COOEt	O	2	1	1	433	94
45.				COOEt	O	2	1	1	432	61
46.				COOEt	O	1	1	1	407	94
47.				COOEt	O	2	1	1	476	100
48.				COOEt	O	1	1	1	471	98
49.				COOEt	O	2	1	1	508	49
50.				COOEt	O	2	1	1	458	92
51.				COOEt	O	2	1	1	492	71
52.				COOEt	O	2	1	1	493	88

53.				COOEt	O	2	1	1	562	82
54.				COOEt	O	2	1	1	564	37
55.				COOEt	O	1	1	1	531	59
56.				COOEt	O	1	1	1	467	94
57.				COOEt	O	2	1	1	534	58
58.				COOEt	O	2	1	1	555	73
59.				COOEt	O	2	1	1	579	44
60.				COOEt	O	2	1	1	518	80
61.				COOEt	O	2	1	1	534	20
62.				COOEt	O	2	1	1	494	78

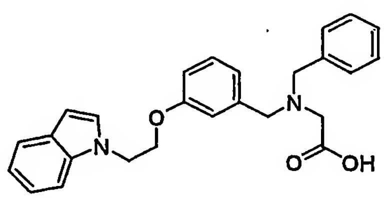
63.				COOEt	O	2	1	1	586	100
	^{1}H: 1.26(3H, t, J=6.15 Hz), 2.04-2.30 (2H, m), 2.36 (3H, s), 3.79 (3H, s), 3.93-3.97 (4H, m), 4.17-4.26 (4H, m), 5.93 (1H, d, J=3.15 Hz), 5.99 (3H, s), 6.04 (1H, d, J=3.3 Hz), 6.66-6.71 (2H, m), 6.84-6.87 (4H, m), 7.05 (2H, d, J=8.73 Hz), 7.17 (2H, d, J=6.48 Hz).									
64.				COOEt	O	2	1	1	504	50
	^{1}H: 1.22-1.25 (3H, m), 3.79 (3H, s), 3.96 (2H, s), 4.13-4.18 (2H, m), 4.54-4.67 (4H, m), 5.11 (2H, t, J=5.50 Hz), 6.85-6.90 (4H, m), 7.01 (2H, d, J=7.2 Hz), 7.20 (2H, d, J=8.59 Hz), 7.38-7.41 (2H, m), 7.86-7.89 (2H,m).									
65.				COOEt	O	2	1	1	586	22
	^{1}H: 1.30 (3H, t, J=7.3 Hz), 2.36 (3H, s), 3.79 (3H, s), 3.93-3.98 (4H, m), 4.10-4.29 (4H, m), 4.56-4.66 (2H, m), 5.93 (1H, d, J=2.85 Hz), 5.98 (2H, s), 6.03 (1H, d, J=3.36 Hz), 6.62-6.68 (2H, m), 6.84-6.87 (6H, m), 7.01-7.25 (3H, m).									
66.				COOEt	O	2	1	1	503	39
	^{1}H: 1.20-1.28 (3H, m), 3.78 (3H, s), 3.96 (2H, s), 4.15-4.18 (2H, m), 4.30-4.32 (2H, m), 4.54 (1H, s), 4.56-4.59 (2H, m), 4.64 (1H, s), 6.81 (2H, d, J=8.49 Hz), 6.85 (2H, d, J=9.15 Hz), 7.02 (2H, d, J=8.97 Hz), 7.22 (2H, d, J=8.58 Hz), 7.26-7.81 (4H, m), 8.06 (1H, s).									
67.				COOEt	O	1	1	1	503	43
	^{1}H: 1.98 (3H, t, J=7.38 Hz), 3.79 (3H, s), 3.89 (3H, s), 3.97 (2H, s), 4.11-4.18 (2H, m), 4.55 (1H, s), 4.66 (1H, s), 5.42 (2H, s), 6.86 (2H, d, J=9.03 Hz), 7.02 (2H, d, J=8.28 Hz), 7.06 (2H, d, J=8.75 Hz), 7.23-7.26 (2H, m), 7.28-7.77 (3H, m), 7.78-7.80 (1H, m).									
68.				COOEt	O	2	1	1	548	20

69.				COOEt	O	1	1	1	533	30
70.				COOEt	O	2	1	1	629	36
71.				COOEt	O	2	1	1	537	33
	^{1}H: 1.24 (3H, t, J=7.11 Hz), 3.19 (3H, s), 3.79 (3H, s), 3.88 (2H, t, J=5.44 Hz), 3.98 (2H, s), 4.15 - 4.19 (4H, m), 4.55 (1H, s), 4.66 (1H, s), 6.69 (2H, d, J=9.33 Hz), 6.81-6.88 (4H, m), 7.04 (2H, d, J=8.79 Hz), 7.22-7.26 (2H, m), 8.13 (2H, d, J=9.39 Hz).									
72.				COOEt	O	2	1	1	562	30
	^{1}H: 1.25 (3H, t, J=6.67 Hz), 2.36 (3H, s), 2.48 (3H, s), 3.79 (3H, s), 3.99 (2H, s), 4.08 (2H, t, J=6.26 Hz), 4.15-4.22 (2H, q, J=7.10 Hz), 4.34 (2H, t, J=6.25 Hz), 4.57 (1H, s), 4.67 (1H, s), 5.91 (1H, d, J=3.37 Hz), 6.18 (1H, d, J=3.41 Hz), 6.72 (2H, d, J=9 Hz), 6.81-6.89 (4H, m), 7.02 (2H, d, J=8.96 Hz), 7.18-7.25 (2H, m).									
73.				COOEt	O	1	1	1	490	26
	^{1}H: 1.23 (3H, t, J=6.67 Hz), 3.79 (3H, s), 3.99 (2H, s), 4.14-4.20 (2H, q, J=7.09 Hz), 4.57 (1H, s), 4.67 (1H, s), 5.32 (2H, s), 6.87 (2H, d, J=6.84 Hz), 7.01-7.08 (4H, m), 7.27 (2H, d, J=6.93 Hz), 7.37 (2H, m), 7.53-7.57 (1H, m), 7.75-7.78 (1H, m).									
74.				COOEt	O	1	1	1	506	78
	^{1}H: 0.8 (3H, m), 3.79 (3H, s), 3.99 (2H, S), 4.14-4.20 (2H, m), 4.57 (1H, s), 4.67 (1H, s), 5.5(2H, s), 6.85-6.88 (2H, m), 7.01-7.05 (4H, m), 7.26-7.28, (2H, m), 7.41 (1H, t, J=7.3 Hz), 7.5 (1H, m), 7.9 (1H, d, J=8.0 Hz), 8.0 (1H, d, J=8.0 Hz).									
75.				COOEt	O	2	1	1	472	41
	^{1}H: 1.25 (3H, t, J=7.1Hz), 2.59 (4H, d, J=4.0 Hz), 2.79-2.83 (2H, m), 3.74 (4H, t, J=4.5 Hz), 3.79 (3H, s), 3.99 (2H, d, J=3.2 Hz), 4.09-4.67 (4H, m), 4.56 (1H, s), 4.67 (1H, s), 6.86-6.91 (4H, m), 7.01-7.07 (2H, m), 7.22-7.26 (2H, m).									

76.				COOEt	O	2	1	1	546	83
	^{1}H: 1.15 (3H, t, J=7.12 Hz), 2.35 (3H, s), 2.48 (3H, s), 3.82 (1H, s), 3.91 (1H, s), 4.03-4.17 (4H, m), 4.33 (2H, t, J=6.42 Hz), 4.50-4.51 (2H, m), 5.17-5.20 (2H, m), 5.91 (1H, d, J=3.18 Hz), 6.17 (1H, d, J=3.42 Hz), 6.68-6.74 (3H, m), 6.80 (1H, d, J=3.42 Hz), 7.05 (1H, d, J=8.4 Hz), 7.14 (1H, d, J=8.46 Hz), 7.330-7.336 (5H, m).									
77.				COOEt	O	2	1	1	544	25
78.				COOEt	O	2	1	1	588	34

Preparation 9

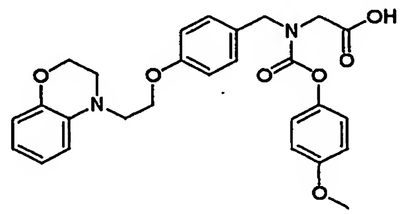
{Benzyl-[3-(2-indol-1-yl-ethoxy)-benzyl]-amino}-acetic acid.
(compound No.87)



To a solution of ethyl-{benzyl-[3-(2-indol-1-yl-ethoxy)-benzyl]-amino}-acetate (compound No.17) (1.0 g) in ethanol (12 mL) was added a solution of sodium hydroxide (130 mg) in water (4 mL) and the reaction mixture was stirred at 30 ^{0}C for 16 hours. The solvent was evaporated under reduced pressure. Water (50 mL) was added to the residue, acidified with 1N HCl to pH 6 and extracted with ethyl acetate (4X30 mL). The combined organic extract was washed with water (50 mL), brine solution (50 mL), dried over sodium sulphate and evaporated under reduced pressure. The crude product was chromatographed (flash) over silica gel using 3.5 % methanol in chloroform as an eluent to obtain 260 mg of pure product.

Preparation 10

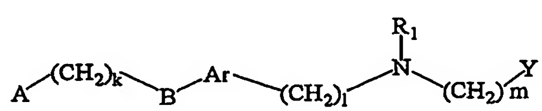
[{4-[2-(2,3-Dihydro-benzo[1,4]oxazin-4-yl)-ethoxy]-benzyl}-(4-methoxy-phenoxycarbonyl)-amino]-acetic acid.(compound No.100)

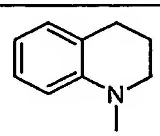
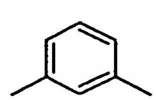
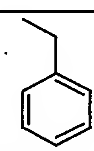


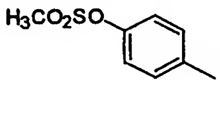
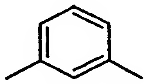
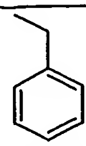
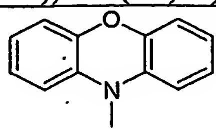
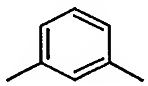
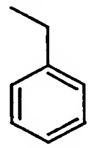
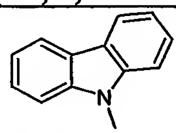
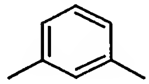
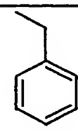
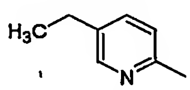
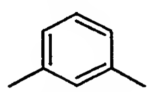
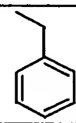
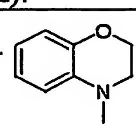
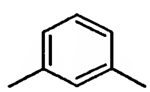
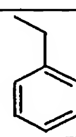
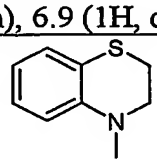
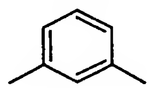
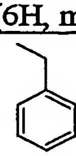
To a solution of ethyl-[{4-[2-(2,3-dihydro-benzo[1,4]oxazin-4-yl)-ethoxy]-benzyl}-(4-methoxy-phenoxycarbonyl)-amino]-acetate (compound No.32) (1.18 g) in a mixture of tetrahydrofuran (4.5 mL) and methanol (1.5 mL) was added a solution of $LiOH.H_2O$ (196 mg) in water (1.5 mL) and the reaction mixture was stirred at ambient temperature for 30 minutes. The solvent was evaporated under reduced pressure, water (50 mL) was added to the residue, acidified with 1N HCl to pH 6 and extracted with ethyl acetate (3X50 mL). The combined organic extract was washed with water (50 mL), brine solution (50 mL), dried over sodium sulphate and evaporated under reduced pressure. The crude product was chromatographed (flash) over silica-gel using 1 % methanol in chloroform as an eluent to obtain 360 mg of pure product.

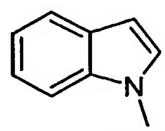
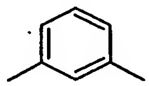
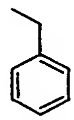
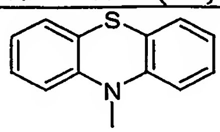
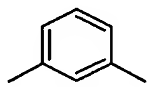
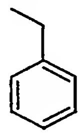
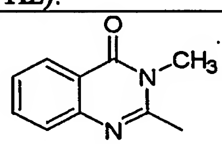
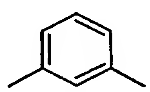
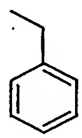
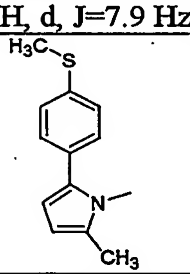
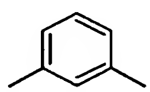
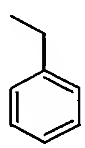
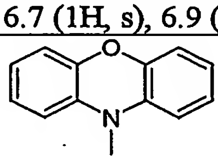
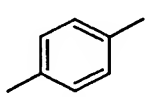
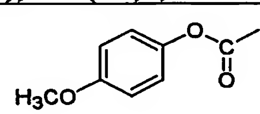
In like manner compounds in table 3 were prepared by a procedure similar to that described in preparation 9 &10.

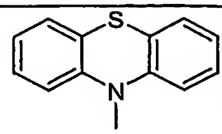
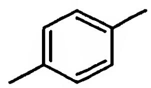
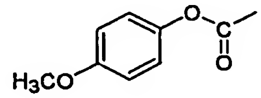
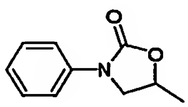
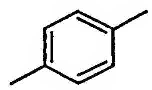
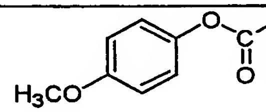
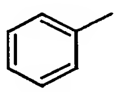
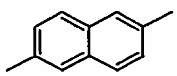
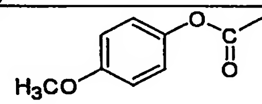
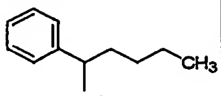
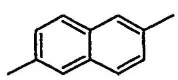
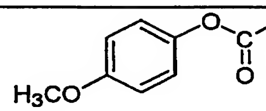
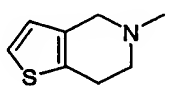
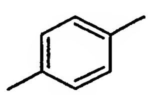
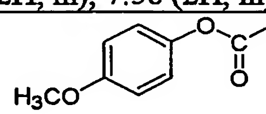
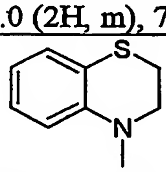
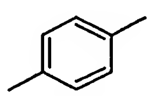
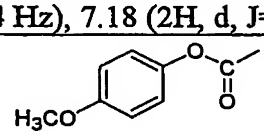
Table 3:

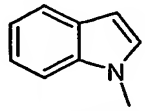
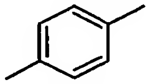
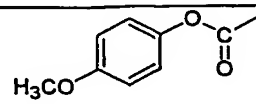
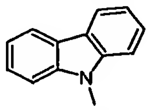
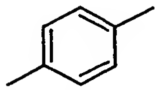
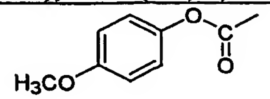
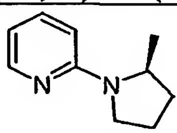
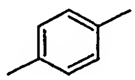
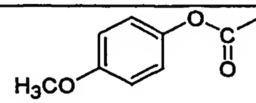
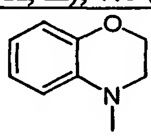
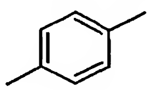
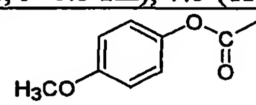
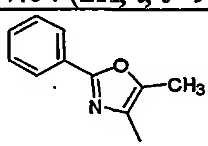
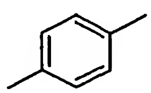
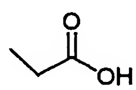
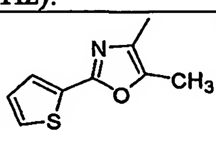
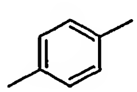
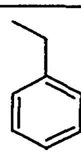


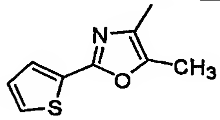
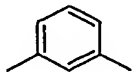
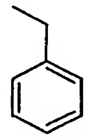
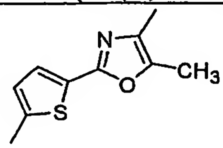
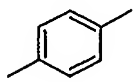
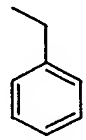
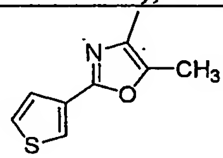
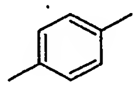
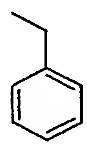
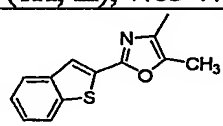
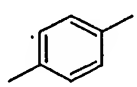
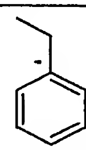
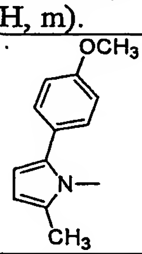
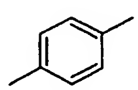
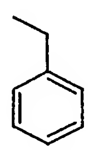
S. No	A	Ar	R_1	Y	B	k	l	m	Mol. Wt.	% Yield
79.				COOH	O	2	1	1	430	24
	^{1}H: 1.94 (2H, t, J=6.93 Hz), 2.75 (2H, t, J=6.17 Hz), 3.26 (2H, s), 3.42 (2H, t, J=5.54 Hz), 3.69 (4H, m), 3.77 (2H, s), 4.13 (2H, t, J=6.10 Hz), 6.59 (2H, m), 6.82 (2H, d, J= 5.73 Hz), 6.88 (1H, d, J=7.5 Hz), 6.94 (1H, d, J=6.96 Hz), 7.05 (1H, t, J=7.56 Hz), 7.22 (6H, complex).									

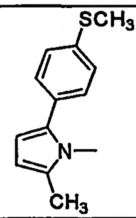
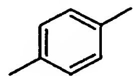
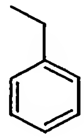
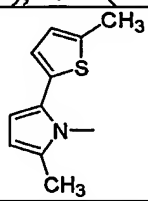
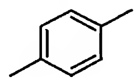
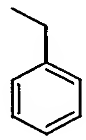
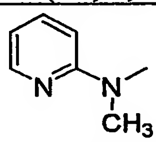
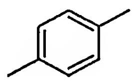
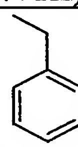
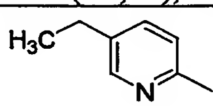
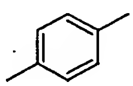
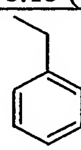
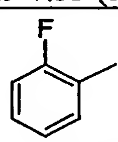
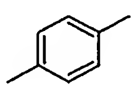
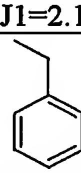
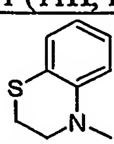
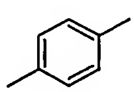
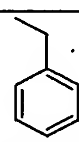
80.				COOH	O	2	1	1	469.	42
	^{1}H: 3.0 (2H, t, J=6.7 Hz), 3.1 (3H,s), 3.2 (2H, s), 3.79 (2H,s), 3.83 (2H, s), 4.1 (2H, t, J=6.7 Hz), 6.9 (3H, m), 7.2 (4H, m), 7.6 (6H,m).									
81..				COOH	O	2	1	1	480	62
	^{1}H: 3.24 (2H, s), 3.77 (2H, s), 3.78 (2H, s), 3.98 (2H, t, J=6.13 Hz), 4.20 (2H, t, J=6.06 Hz), 6.64 (5H, m), 6.79 (3H, dd, J=15.52&7.06 Hz), 6.97 (2H, d, J=6.24 Hz), 7.25 (4H, m), 7.36 (2H, d, J=6.93 Hz), 7.58 (1H, s).									
82.				COOH	O	2	1	1	464	85
	DMSO-D$_6$, ^{1}H: 3.10 (2H, s), 3.62 (2H, s), 3.65 (2H, s), 4.33 (2H, t, J=5.10 Hz), 4.79 (2H, t, J=5.07 Hz), 6.67 (1H, dd, J=1.87& 8.085 Hz), 6.78 (1H, s), 6.84 (1H, d, J=7.43 Hz), 7.11-7.23 (4H, m), 7.11-7.23 (4H, m), 7.44 (2H, t, J=7.18 Hz), 7.68 (2H, d, J= 8.25 Hz). 8.12 (2H, d, J=7.68 Hz).									
83.				COOH	O	2	1	1	404	64
	^{1}H: 1.24 (3H, t, J=15.3 Hz), 2.63 (2H, q, J=15.18 & 7.56 Hz), 3.22 (2H, t, J=6.91 Hz), 3.27 (2H, s), 3.74 (2H, s), 3.81 (2H, s), 4.34 (2H, t, J=6.93 Hz), 6.83 (2H, m), 6.95 (1H, s), 7.21 (2H, dd, J=7.86 & 2.25 Hz), 7.33 (5H, m), 7.5 (1H, d, J= 6.82 & 2.13 Hz), 8.4 (1H, d, J=1.62 Hz).									
84.				COOH	O	2	1	1	432	86
	^{1}H: 3.28 (2H, s), 3.5 (2H, t, J=4.5 Hz), 3.69 (2H, t, J=5.6Hz), 3.75 (2H, s), 3.79 (2H, s), 4.1 (2H, t, J=5.6 Hz), 4.2 (2H, t, J=4.3 Hz), 6.6 (1H, m), 6.7 (1H, d, J=7.0 Hz), 6.77-6.83 (4H, m), 6.9 (1H, d, J=7.58 Hz), 7.2 - 7.35 (6H, m).									
85.				COOH	O	2	1	1	448	92
	^{1}H: 3.0 (2H, t, J= 4.66 Hz), 3.3 (2H, s), 3.7 (4H, m), 3.79 (2H, s), 3.83 (2H, s), 4.1 (2H, t, J=5.58 Hz), 6.6 (1H, t, J=7.3 Hz), 6.7 (1H, d, J= 8.2 Hz), 6.8-7.0 (5H, m), 7.2-7.32 (6H, m).									

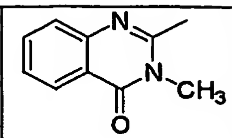
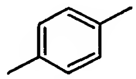
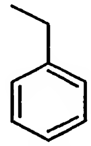
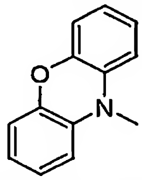
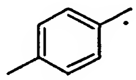
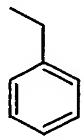
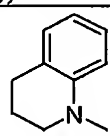
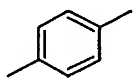
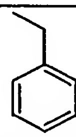
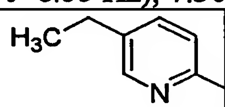
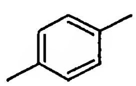
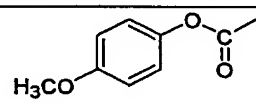
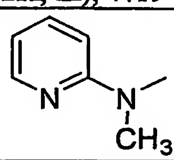
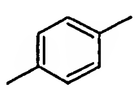
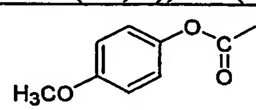
86.				COOH	O	2	1	1	414	58
	^{1}H: 3.25 (2H, s), 3.7 (2H, s), 3.75 (2H, s), 4.26 (2H, t, J=5.56 Hz), 4.52 (2H, t, J=5.5 Hz), 6.5 (1H, d, J=3.07 Hz), 6.7 (2H, d, J=7.45 Hz), 6.8 (1H, d, J=7.43 Hz), 7.1 (1H, t, J=7.03 Hz), 7.20 - 7.38 (7H, m), 7.4 (2H, d, J=8.26 Hz), 7.6 (1H, d, J=7.8 Hz).									
87.				COOH	O	3	1	1	510	94
	^{1}H: 2.26 (2H, m), 3.24 (2H, s), 3.75 (2H, s), 3.79 (2H, s), 4.0 (4H, t, J=6.07 Hz), 6.7 (1H, d, J=8.3 Hz), 6.88 - 6.96 (6H, m), 7.10 - 7.20 (5H, m), 7.22 - 7.32 (3H, m), 7.38 (2H, d, J=7.19 Hz).									
88.				COOH	O	1	1	1	443	88
	^{1}H: 3.2 (2H, s), 3.7 (3H, s), 4.1(2H, s), 4.2 (2H, s), 5.3 (2H, s), 7.1 (2H, t, J=9.6 Hz), 7.2 (1H, s), 7.3 - 7.4 (6H, m), 7.5 (1H, t, J=7.3 Hz), 7.69 (1H, d, J=8.1 Hz), 7.7 (1H, t, J=7.5 Hz), 8.2 (1H, d, J=7.9 Hz).									
89.				COOH	O	2	1	1	500	100
	^{1}H: 2.3 (3H, s), 2.5 (3H, s), 3.2 (2H, s), 3.7 (2H, s), 3.8 (2H, s), 3.9 (2H, t, J=6.4 Hz), 4.3 (2H, t, J=6.4 Hz), 5.9 (1H, d, J=3.2 Hz), 6.1 (1H, d, J=3.4 Hz), 6.6 (1H, dd, J=8.2 & 2.1 Hz), 6.7 (1H, s), 6.9 (1H, d, J=7.7 Hz), 7.2 (2H, t, J=7.9 Hz), 7.3 (3H, m), 7.35 (5H, m).									
90.				COOH	O	2	1	1	540	71
	^{1}H: 3.78 (3H, s), 3.9 (2H, m), 4.03 (2H, d, J=4.26 Hz), 4.19 (2H, m), 4.57 (1H, s), 4.67 (1H, s), 6.61- 6.7 (6H, m), 6.7-6.0(6H, m), 7.04 (2H, t, J=9.3 Hz), 7.2 (2H, d, J=10.26 Hz).									

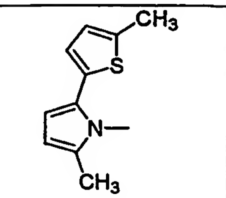
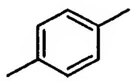
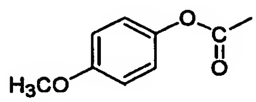
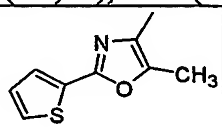
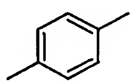
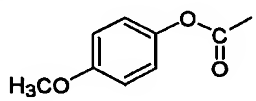
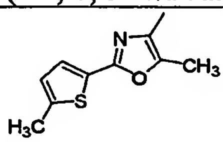
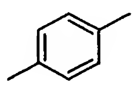
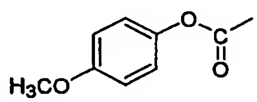
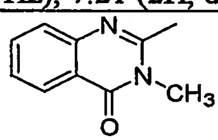
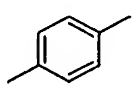
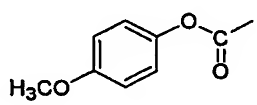
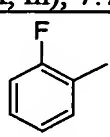
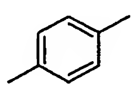
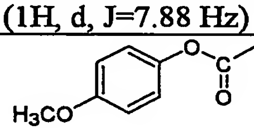
91.				COOH	O	2	1	1	556	59
	^{1}H: 3.78 (3H, s), 4.04 (2H, d, J=4.86 Hz), 4.31 (4H, s), 4.56 (1H, s), 4.6 (1H, s), 6.85-6.91 (4H, m), 6.96 (3H, d, J=7.2 Hz), 7.04 (3H, t, J=8.7 Hz), 7.13 (3H, d, J=7.57 Hz), 7.18-7.23 (3H, m).									
92.				COOH	O	1	1	1	506	62
	^{1}H: 3.78 (3H, s), 4.08 (3H, m), 4.16-4.25 (3H, m), 4.57 (1H, s), 4.67 (1H, s), 4.98 (1H, m), 6.84-6.93 (4H, m), 7.04 (2H, t, J=8.64 Hz), 7.18 (1H, t, J=7.4 Hz), 7.27 (2H, m), 7.39 (2H, t, J=7.9 Hz), 7.5 (2H, d, J=7.9 Hz).									
93.				COOH	O	1	1	1	471	86
	^{1}H: 3.79 (3H, s), 4.09 (2H, s), 4.7 (1H, s), 4.87 (1H, s), 5.18 (2H, s), 6.87 (2H, d, J=8.7 Hz), 7.08 (2H, t, J=8.9 Hz), 7.24 (2H, m), 7.32-7.43 (4H, m), 7.50 (2H, d, J=7.3 Hz), 7.63 (1H, s), 7.73 (2H, t, J=8.0 Hz).									
94.				COOH	O	0	1	1	527	70
	^{1}H: 0.9 (3H, t, J=6.8 Hz),1.25-1.5 (4H, m), 1.89 (1H, m), 2.04 (1H, m), 3.7 (3H, s), 4.03 (2H, s), 4.71 (1H, s), 4.8 (1H, s), 5.25 (1H, t, J=5.8 Hz), 6.85 (2H, d, J=8.5 Hz), 7.0-7.08 (3H, m), 7.2 (2H, m), 7.32 (3H, m), 7.4 (2H, m), 7.58 (2H, m), 7.69 (1H, d, J=8.91Hz).									
95.				COOH	O	2	1	1	496	50
	^{1}H: 3.03 (2H, t, J=5.3 Hz), 3.24 (4H, m), 3.7 (3H, s), 3.86 (2H, d, J=6.84 Hz), 4.01 (2H, s), 4.25 (2H, t, J=5.3 Hz), 4.52 (1H, s), 4.6 (1H, s), 6.74 (1H, d, J=5.14 Hz), 6.81-6.87 (4H, m), 7.0 (2H, m), 7.14 (1H, d, J=5.14 Hz), 7.18 (2H, d, J=7.9 Hz).									
96.				COOH	O	2	1	1	508	52
	^{1}H: 3.04 (2H, t, J=5.0 Hz), 3.74-3.79 (7H, complex), 4.04 (2H, d, J=4.98 Hz), 4.17 (2H, t, J=4.66 Hz), 4.56 (1H, s), 4.67 (1H, s), 6.62 (1H, t, J=7.33 Hz), 6.72 (1H, d, J=8.16 Hz), 6.87 (4H, t, J=6.21 Hz), 6.96-7.07 (4H, m), 7.21 (2H, m).									

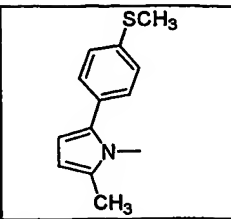
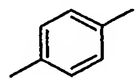
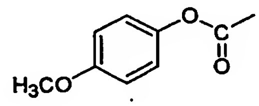
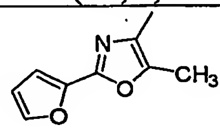
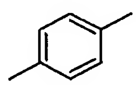
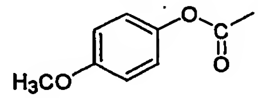
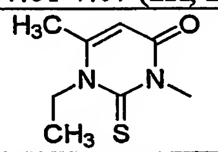
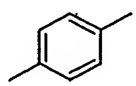
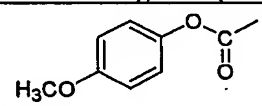
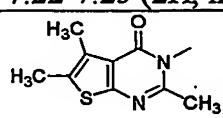
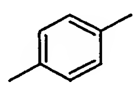
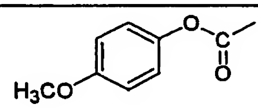
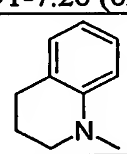
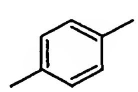
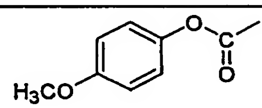
97.				COOH	O	2	1	1	474	15
	^{1}H: 3.78 (3H, s), 4.0 (2H, d, J=3.24 Hz), 4.27 (2H, t), 4.54 (3H, m), 4.64 (1H, s), 6.51 (1H, d, J=2.76 Hz), 6.52-6.88 (4H, m), 7.03 (2H, t, J=8.8 Hz), 7.1 (1H, t, J=7.42 Hz), 7.21 (4H, t, J=5.86 Hz), 7.41 (1H, d, J=8.16 Hz), 7.63 (1H, d, J=7.8 Hz).									
98.				COOH	O	2	1	1	524	48
	^{1}H: 3.8 (3H, s), 4.0 (2H, s), 4.3 (2H, m), 4.5 (1H, s), 4.6 (1H, s), 4.7 (2H, t, J=4.8 Hz), 6.8 (2H, t, J=7.4 Hz), 6.9 (2H, m), 7.0 (2H, t, J=8.6 Hz), 7.1 (2H, d, J=8.2 Hz), 7.2 (2H, m), 7.5 (4H, m) 8.1 (2H, d, J=7.8Hz).									
99.				COOH	O	1	1	1	491	48
	^{1}H: 2.1(2H, m), 2.2 (2H, m), 3.3 (2H, m), 3.8 (3H, s), 3.85 (1H, m), 3.9 (2H, d, J=10.5 Hz) 4.2 (1H, m), 4.4 (1H, m), 4.5 (1H, s), 4.6 (1H, s), 6.5 (1H, d, J=8.5 Hz), 6.6 (1H, m), 6.8 (4H, m), 7.0 (2H, m), 7.2 (2H, d, J=8.5 Hz), 7.5 (1H, m), 8.1 (1H, d, J=4.3 Hz).									
100.				COOH	O	2	1	1	492	31
	^{1}H: 3.51 (2H, s), 3.70 (2H, d, J=5.39 Hz), 3.78 (3H, s), 4.0(2H,d,J=5.4 Hz), 4.15-4.2 (4H, m), 4.56 (1H, s),4.66 (1H,s),6.6 (1H, t, J=7.0 Hz), 6.7 (1H, d, J=7.9 Hz),6.79-6.86 (6H, m), 7.04 (2H, t, J=9.54 Hz),7.2 (2H, d, J=8.52 Hz).									
101.				COOH	O	2	1	1	424	73
	DMSO-d6, ^{1}H: 3.35 (3H, s), 2.91 (2H, t, J=6.2 Hz), 3.35 (4H, s), 3.93 (2H, s), 4.2 (2H, t, J=6.3 Hz), 6.86 (2H, d, J=8.2 Hz), 7.22 (2H, d, J=8.2 Hz), 7.35 (3H, m), 7.9 (2H, d, J=7.35 Hz).									
102.				COOH	O	2	1	1	462	84
	^{1}H: 2.34 (3H, s), 2.95 (2H, t, J=6.51 Hz), 3.29 (2H, s), 3.81 (2H, s), 3.84 (2H, s), 4.20 (2H, t, J=6.58 Hz), 6.86 (2H, d, J=8.49 Hz), 7.05-7.08 (1H, m), 7.21-7.36 (8H, m), 7.57-7.58 (1H, d, J=3.12 Hz).									

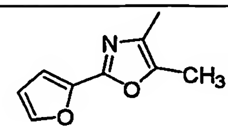
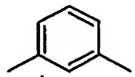
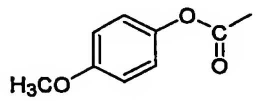
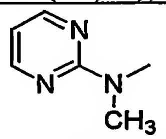
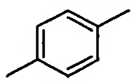
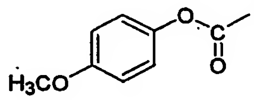
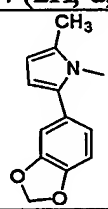
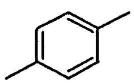
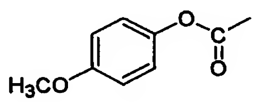
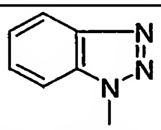
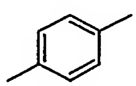
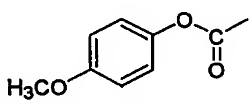
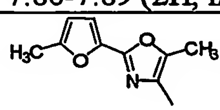
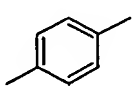
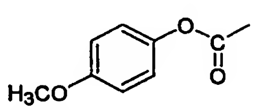
103.				COOH	O	2	1	1	462	85
	DMSO-d_6 ^{1}H: 2.30 (3H, s,), 2.88 (2H, t, J=6.28 Hz), 3.14 (2H , s), 3.68 (2H, s), 3.70(s,2H), 4.15 (2H, t, J=6.40 Hz), 6.7-6.9 (3H , m), 7.06-7.3 (7H , m), 7.58-7.86 (2H, m).									
104.				COOH	O	2	1	1	476	40
	^{1}H: 2.33 (3H, s), 2.50 (3H,s), 2.93 (2H, t, J=6.57 Hz), 3.26 (2H, s), 3.74 (2H, s), 3.78 (2H, s), 4.20 (2H, t, J=6.63 Hz), 6.71 (1H, d, J=2.67Hz), 6.85 (2H, d, J=8.49 Hz), 7.18 (2H, d, J=8.49 Hz), 7.28-7.37 (6H, m).									
105.				COOH	O	2	1	1	462	45
	^{1}H: 2.34 (3H, s), 2.96 (2H, t, J=6.58 Hz), 3.26 (2H, s), 3.75 (2H, s), 3.79 (2H, s), 4.21 (2H, t, J=6.62 Hz), 6.86 (2H, d, J=8.54 Hz), 7.18 (2H, d, J=8.52 Hz), 7.28-7.37 (6H, m), 7.55-7.57 (1H, m), 7.83-7.84 (1H, m).									
106.				COOH	O	2	1	1	512	25
	^{1}H: 2.39 (3H,s), 2.98 (2H, t, J=6.48 Hz), 3.25 (s, 2H), 3.72 (2H, s), 3.77 (2H, s), 4.24 (2H, t, J=6.55 Hz), 6.87 (2H, d, J=8.53 Hz) 7.18 (2H, d, J=8.53 Hz), 7.30-7.40 (7H, m), 7.79-7.85 (3H, m).									
107.				COOH	O	2	1	1	484	46
	^{1}H: 2.36 (3H, s), 3.25 (2H, s), 3.74 (3H, s), 3.79 (2H, s), 3.83 (2H, s), 3.92 (2H, t, J=6.51 Hz), 4.25 (2H, t, J=6.51 Hz), 5.95 (1H, d, J=2.79 Hz), 6.05 (1H, d, J=3.3 Hz), 6.67 (2H, d, J=8.55 Hz), 6.95 (2H, d, J=8.73 Hz), 7.16 (2H, d, J=8.55 Hz), 7.25-7.3 (3H, m), 7.31-7.33 (4H, m).									

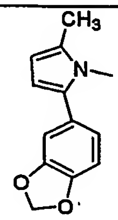
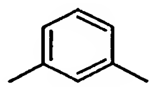
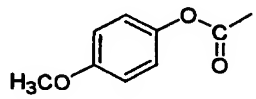
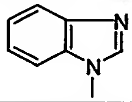
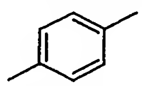
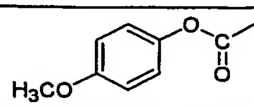
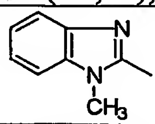
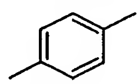
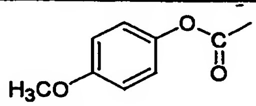
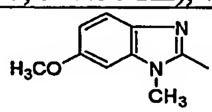
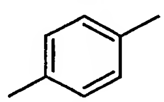
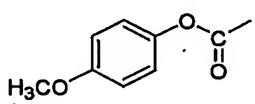
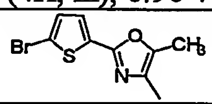
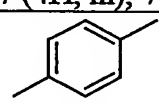
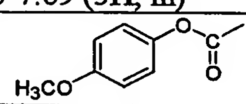
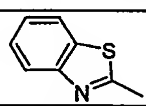
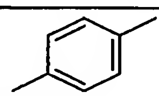
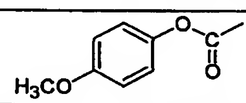
108.				COOH	O	2	1	1	500	53
	[1]H: 2.36 (3H, s), 2.5 (3H, s), 3.26 (2H, s), 3.76 (2H, s), 3.81(2H, s), 3.92 (2H , t, J=6.46 Hz), 4.27 (2H, t, J=6.46 Hz), 5.96 (1H d, J=3.15 Hz), 6.09 (1H, d, J=3.36 Hz) 6.65 (2H, d, J=8.55 Hz), 7.17 (2H, d, J=8.55 Hz), 7.29-7.37 (9H , m).									
109.				COOH	O	2	1	1	474	61
	[1]H: 2.35 (3H, s), 2.48 (3H, s), 3.24 (2H, s), 3.69 (2H, s), 3.74 (2H, s), 4.07 (2H, t, J=6.2 Hz), 4.34 (2H, t, J=6.4 Hz) 5.9 (1H, d, J=3.0 Hz), 6.18 (1H, d, J=3.4 Hz), 6.70 (1H, d, J=2.3 Hz), 6.77 (2H, d, J=8.5 Hz), 6.8 (1H, d, J=3.4 Hz), 7.14 (2H, d, J=8.5 Hz), 7.29-7.38 (5H, m).									
110.				COOH	O	2	1	1	405	61
	[1]H: 3.14 (3H, s), 3.25 (2H, s), 3.72 (2H, s), 3.77 (2H, s), 3.98 (2H, t, J=5.58 Hz), 4.18 (2H, t, J=5.55 Hz), 6.5 (2H, d; J=8.55 Hz), 6.89 (2H, d, J=8.31 Hz), 7.26 (2H, d, J=8.37 Hz), 7.3-7.33 (4H, m), 7.42-7.47 (2H, m), 8.14-8.15 (1H, m).									
111.				COOH	O	2	1	1	404	84
	[1]H: 1.24 (3H, t, J=6.99 Hz), 2.64 (2H, q, J=7.9 Hz), 3.23 (2H, t, J=6.6 Hz), 3.28 (2H, s), 3.8 (2H, s), 3.84 (2H, s), 3.99 (2H, t, J=6.61 Hz), 6.87 (2H, d, J=8.58 Hz), 7.18-7.29 (3H, m), 7.29-7.33 (5H, m), 7.45-7.49 (1H, dd, J1=2.16 Hz, J2=7.92 Hz), 8.4 (1H, s).									
112.				COOH	O	1	1	1	379	56
	[1]H: 3.38 (2H, s), 3.76 (2H, s), 3.80 (2H, s), 5.12 (2H, s), 6.97 (2H, d, J=8.58 Hz) , 7.05-7.51 (11H, m)									
113.				COOH	O	2	1	1	448	57
	[1]H: 3.04 (2H, t, J=6.06 Hz), 3.25 (2H, s), 3.72 (2H, s), 3.76 (2H, s), 3.74-3.79 (4H, m), 4.16 (2H, t, J=5.77 Hz), 6.59-6.61 (1H, m), 6.73 (1H,d, J=7.36 Hz), 6.88 (2H, d, J=8.556 Hz), 6.98-7.04 (2H, m), 7.21 (2H, d, J=8.52 Hz), 7.27-7.37 (5H, m)									

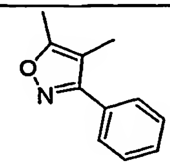
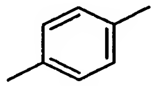
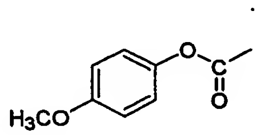
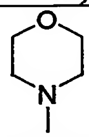
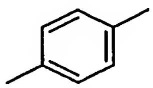
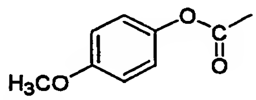
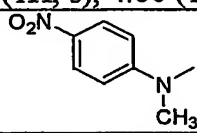
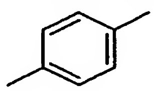
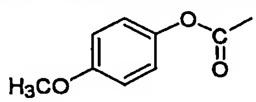
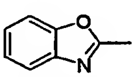
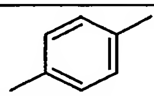
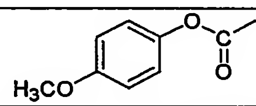
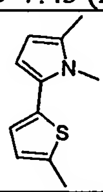
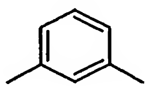
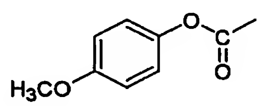
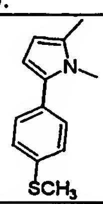
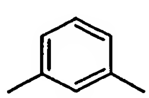
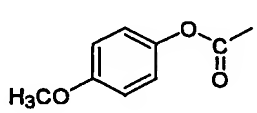
114.				COOH	O	1	1	1	443	76
	DMSO-d6, ^{1}H: 3.14 (3H, s), 3.326 (2H, s), 3.66 (2H, s), 3.70 (2H, s), 5.24(2H, s), 7.08 (2H, d, J=8.58 Hz) , 7.22-7.32 (7H, m), 7.55 (1H, t, J=7.52 Hz), 7.65 (1H, d, J=8.05 Hz), 7.79-7.94 (1H, m), 8.15 (1H, d, J=7.93 Hz).									
115.				COOH	O	2	1	1	480	74
	DMSO-d6, ^{1}H: 3.1 (3H, s), 3.63 (2H, s), 3.68 (2H, s), 3.99 (2H, t, J=5.56 Hz) 4.17 (2H, t, J=5.6 Hz), 6.61-6.63 (4H, m), 6.68-6.81 (2H, m), 6.88 (2H, d, J=8.5 Hz), 7.23 (3H, d, J=8.5 Hz), 7.23-7.31 (5H, m).									
116.				COOH	O	2	1	1	430	53
	^{1}H: 1.94 (2H, qui, J=6.10 Hz), 2.75 (2H, t, J=6.27 Hz), 3.28 (2H, s), 3.42 (2H, t, J=5.51 Hz), 3.69 (2H, t, J=6.06 Hz), 3.79 (2H, s), 3.82 (2H, s), 4.13 (2H, t, J=6.09 Hz), 6.55-6.63 (2H, m) , 6.86 (2H, d, J=8.58 Hz), 6.94 (1H, d, J=7.11 Hz), 7.01-7.07 (1H, m), 7.22 (2H, d, J=8.55 Hz), 7.30-7.38 (5H, m).									
117.				COOH	O	2	1	1	464	87
	^{1}H: 1.25 (3H, t, J=7.59 Hz), 2.68 (2H, q, J=7.57 Hz), 3.78 (2H, t, J=5.7 Hz), 3.78 (3H, s), 3.9 (2H, s), 4.3 (2H, t, J=5.74 Hz) 4.58 (1H, s), 4.67(1H, s), 6.83-6.88 (4H, m), 7.04-7.08 (2H, m), 7.19-7.22 (2H, m), 7.27-7.3 (1H,m), 7.6 (1H, dd, J=2.16 & 7.92 Hz), 8.5 (1H,s)									
118.				COOH	O	2	1	1	465	73
	^{1}H: 3.14 (3H, s), 3.75 (3H, s), 3.94-3.96 (4H, m), 4.14 (2H, s), 4.5 (1H, s), 4.6 (1H, s), 6.56-6.6 (2H, m), 6.77-6.84 (4H, m), 7.03 (2H, d, J=8.9 Hz), 7.19 (2H, d, J=8.2 Hz), 7.48-7.53 (1H, m), 8.15 (1H, s)									

119.				COOH	O	2	1	1	534	96
	^{1}H: 2.35 (3H, s), 2.48 (3H, s), 3.78 (3H, s), 4.03 (2H, t, J=5.83 Hz), 4.07 (2H, s), 4.34 (2H, t, J=5.34 Hz), 4.54 (1H, s), 4.64 (1H, s), 5.91 (1H, d, J=2.97 Hz), 6.18 (1H, d, J=3.3 Hz), 6.69 (1H, d, J=2.3 Hz), 6.74-6.79 (2H, m), 6.82 (1H, d, J=3.27 Hz), 6.84-6.88 (2H, m), 7.00-7.06 (2H, m), 7.20 (2H, d, J=8.07 Hz).									
120.				COOH	O	2	1	1	522	84
	^{1}H: 2.35 (3H, s), 2.96 (2H, t, J=6.48 Hz), 3.77 (3H, s), 4.02 (2H, s), 4.18-4.21 (2H, m), 4.55 (1H, s), 4.64 (1H, s), 6.83-6.89 (4H, m), 7.01-7.08 (3H, m), 7.20 (2H, d, J=7.5 Hz), 7.35 (1H, d, J=4.14 Hz), 7.59 (1H, d, J=3.54 Hz).									
121.				COOH	O	2	1	1	536	35
	^{1}H: 2.35 (3H, s)), 2.49 (3H, s), 2.96 (2H, s), 3.77 (3H, s), 4.0 (2H, s), 4.18 (2H, t, J=6.4 Hz), 4.54 (1H, s), 4.64 (1H, s), 6.82 (1H, d, J=3.08 Hz), 6.72-6.87 (4H, m), 7.03 (2H, d, J=8.6 Hz), 7.21 (2H, d, J=8.29 Hz), 7.41 (1H, d, J=3.58 Hz)									
122.				COOH	O	1	1	1	503	81
	^{1}H: 3.75 (3H, s), 3.78 (3H, s), 4.04 (2H, d, J=4.87 Hz), 4.57 (1H, s), 4.67 (1H, s), 5.20 (2H, s), 6.83-6.87 (2H, dd, J1=5.14Hz, J2=8.85 Hz), 7.00-7.07 (4H, m), 7.28 (2H, s), 7.49-7.54 (1H, m), 7.71-7.79 (2H, m), 8.3 (1H, d, J=7.88 Hz)									
123.				COOH	O	1	1	1	439	85
	^{1}H: 3.76 (3H, s), 4.05 (2H, d, J=10.68 Hz), 4.56 (1H, s), 4.65 (1H, s), 5.12 (2H, s), 6.86 (2H, d, J=8.7 Hz), 6.94-7.49 (10H, m).									

124.				COOH	O	2	1	1	560	80
	^{1}H: 2.37 (3H, s), 2.50 (3H, s), 3.77 (3H, s), 3.95 (2H, t, J=6.09 Hz), 4.02 (2H, d, J=8.43 Hz), 4.28 (2H, t, J=6.06 Hz), 4.53 (1H, s), 4.62 (1H, s), 5.96 (1H, d, J=3.12 Hz), 6.10 (1H, d, J=3.36 Hz), 6.63-6.68 (2H, m), 6.84-6.87 (2H, dd, J=2.73 & 9.00 Hz), 7.00-7.06 (2H, m), 7.15 (2H, d, J=7.22 Hz), 7.28-7.33 (4H, m).									
125.				COOH	O	2	1	1	506	77
	^{1}H: 2.36 (3H, s), 2.97 (2H, t, J=5.15 Hz), 3.77 (3H, s), 4.01 (2H, s), 4.22 (2H, t, J=5.8 Hz), 4.55 (1H, s), 4.63 (1H, s), 6.48-6.50 (1H, m), 6.83-6.88 (4H, m), 6.96 (1H, d, J=3.37 Hz), 7.01-7.07 (2H, m), 7.21 (2H, d, J=8.04 Hz), 7.5 (1H, s).									
126.				COOH	O	2	1	1	527	63
	^{1}H: 1.34 (3H, t, J=7.07 Hz)), 2.36 (3H, s), 3.5 (2H, t, J=6.07 Hz), 3.77 (3H, s), 4.04 (2H, d, J=6.74 Hz), 4.26 (2H, t, J=6.94 Hz), 4.37 (2H, q, J=7.04 Hz), 4.56 (1H, s), 4.66 (1H, s), 6.23 (1H, s), 6.87 (2H, dd, J=3.19 & 5.82 Hz), 6.94 (2H, t, J=7.6 Hz), 7.04 (2H, t, J=8.23 Hz), 7.22-7.25 (2H, m).									
127.				COOH	O	2	1	1	551	80
	^{1}H: 2.37 (3H, s), 2.39 (3H, s), 2.68 (3H, s), 3.77 (3H, s), 4.08 (2H, d, J=10.77 Hz), 4.36 (2H, t, J=4.45 Hz), 4.58 (1H, s), 4.67 (1H, s), 4.83 (2H, t, J=4.47 Hz), 6.87 (2H, d, J=7.62 Hz), 6.91-7.26 (6H, m)									
128.				COOH	O	2	1	1	490	83
	^{1}H: 1.95 (2H, qui, J=5.94 Hz), 2.76 (2H, t, J=6.27 Hz), 3.43 (2H, t, J=5.49 Hz), 3.69 (2H, t, J=5.67 Hz), 3.78 (3H, s), 4.03 (2H, t, J=5.28 Hz), 4.14 (2H, t, J=4.98 Hz), 4.56 (1H, s), 5.66 (1H, s), 6.56-6.64 (2H, m), 6.84-6.89 (4H, m), 6.95(1H, d, J=7.68 Hz), 7.01-7.07 (3H, m), 7.22 (2H, d, J=8.22 Hz).									

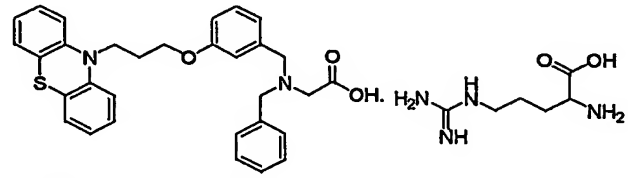
129.				COOH	O	2	1	1	506	63
	^{1}H: 2.36 (3H, s), 2.96 (2H, t, J=7.37 Hz), 3.76 (3H, s), 4.07 (2H, s), 4.28 (2H, t, J=7.25 Hz), 4.63 (1H, s), 4.69 (1H, s), 6.48-6.50 (1H, m), 6.81-6.85 (4H, m), 6.98-7.07 (4H, m), 7.08-7.24 (1H, m), 7.50-7.51 (1H, m).									
130.				COOH	O	2	1	1	466	90
	^{1}H: 3.25 (3H, s), 3.78 (3H, s), 4.01-4.03 (4H, m), 4.21 (2H, t, J=5.5 Hz), 4.55 (1H, s), 4.65 (1H, s), 6.49-6.52 (1H, m), 6.84-6.89 (4H, m), 7.01-7.07 (2H, m), 7.22 (2H, d, J=7.83 Hz), 8.34 (2H, d, J=4.8Hz).									
131.				COOH	O	2	1	1	558	72
	^{1}H: 2.36 (3H, s), 3.77-3.83 (2H, m), 3.94-4.00 (2H, m), 4.07 (3H, s), 4.20-4.27 (2H, m), 4.50-4.60 (2H, m), 5.92 (1H, d, J=3.00 Hz), 5.98 (2H, s), 6.03 (1H, d, J=3.30 Hz), 6.65-6.70 (3H, m), 6.85-6.88 (4H, m), 7.02 (2H, d, J=8.98 Hz), 7.13-7.17 (2H, m)									
132.				COOH	O	2	1	1	476	62
	^{1}H: 3.76 (3H, s), 4.08 (2H, s), 4.53 (2H, s), 4.64 (2H, t, J=5.59 Hz), 5.10 (2H, t, J=5.52 Hz), 6.82-6.85 (4H, m), 7.00 (2H, d, J=8.80 Hz), 7.19 (2H, d, J=8.07 Hz), 7.37-7.41 (2H, m), 7.86-7.89 (2H, m).									
133.				COOH	O	2	1	1	520	81
	^{1}H: 2.37 (3H, s), 2.42 (3H, s), 2.96 (2H, t, J=5.65 Hz), 4.02 (2H, s), 3.78 (3H, s), 4.20 (2H, t, J=5.64 Hz), 4.55 (1H, s), 4.65 (1H, s), 6.08 (1H, d, J=2.63 Hz), 6.83-6.91 (5H, m), 7.01-7.07 (2H, m), 7.20 (2H, d, J=8.30 Hz).									

134.				COOH	O	2	1	1	558	84
	¹H: 2.49 (3H, s), 3.72 (3H, s), 3.97 (2H, s), 4.20-4.22 (2H, m), 4.25-4.39 (2H, m), 4.55 (2H, s), 5.80 (1H, d, J=3.18 Hz), 5.89 (1H, d, J=3.12 Hz), 6.02 (2H, s), 6.64-6.67 (2H, m), 6.81-7.01 (8H, m), 7.17-7.20 (1H, m).									
135.				COOH	O	2	1	1	475	64
	¹H: 3.78 (3H, s), 4.04 (2H, s), 4.38-4.39 (2H, s), 4.53-4.56 (3H, m), 4.66 (1H, s), 6.62 (2H, d, J=8.28 Hz), 6.85 (2H, d, J=8.94 Hz), 7.06 (2H, d, J=9.03 Hz), 7.18 (2H, d, J=8.55 Hz), 7.32-7.39 (2H, m), 7.47 (1H, d, J=7.47 Hz), 7.80 (1H, d, J=7.8 Hz), 8.02 (1H, s).									
136.				COOH	O	1	1	1	475	69
	¹H: 3.78 (3H, s), 3.93 (3H, s), 4.05 (2H, s), 4.60 (1H, s), 4.71 (1H, s), 5.51 (2H, s), 6.85 (2H, d, J=7.38 Hz), 7.03-7.09 (4H, m), 7.27 (2H, m), 7.31-7.83 (4H, m)									
137.				COOH	O	1	1	1	505	50
	¹H: 3.77 (3H, s), 3.87 (6H, s), 4.05 (2H, s), 4.60 (1H, s), 4.70 (1H, s), 5.42 (2H, s), 6.79-6.87 (4H, m), 6.90-7.07 (4H, m), 7.26-7.69 (3H, m)									
138.				COOH	O	2	1	1	601	23
	¹H: 2.34 (3H, s), 2.94 (2H, t, J=5.95 Hz), 3.78 (3H, s), 4.03 (2H, s), 4.19 (2H, s), 4.56 (1H, s), 4.65 (1H, s), 6.84-6.87 (4H, m), 7.03-7.07 (3H, m), 7.2 (2H, d, J=8.31 Hz), 7.32 (1H, m)									
139.				COOH	O	1	1	1	478	90
	¹H: 3.78 (3H, s), 4.04 (2H, s), 4.58 (2H, s), 5.5 (2H, s), 6.86 (2H, d, J=8.1 Hz), 7.0-7.03 (4H, m), 7.26-7.29 (2H, m), 7.38-7.43 (1H, m), 7.48-7.53 (1H, m), 7.89 (1H, d, J=8.0 Hz), 8.03 (1H, d, J=8.1 Hz)									

140.				COOH	O	2	1	1	516	30
	^{1}H: 2.43 (3H, s), 2.89 (2H, m), 3.48 (2H, s), 3.63 (3H, s), 3.93 (2H, m), 4.35 (1H, s), 4.50 (1H, s), 6.71 (2H, d, J=6.9 Hz), 6.84 (2H, d, J=7.92 Hz), 6.96 (2H, t, J=8.4 Hz), 7.10 (2H, t, J=9.33 Hz), 7.49 (3H, s), 7.62 (2H, d, J=3.18 Hz)									
141.				COOH	O	2	1	1	444	31
	^{1}H: 2.87 (4H, s), 3.02 (2H, m), 3.7 (3H, s), 3.80 (4H, s), 3.91 (2H, s), 4.18 (2H, m), 4.53 (1H, s), 4.60 (1H, s), 6.80-6.86 (4H, m), 7.03 (2H, d, J=8.94 Hz), 7.19 (2H, d, J= 8.31 Hz)									
142.				COOH	O	2	1	1	509	85
	^{1}H: 3.15 (3H, s), 3.70 (3H, s), 3.81-3.89 (4H, m), 4.08 (2H, t, J=5.49 Hz), 4.48 (1H, s), 4.52 (1H, s), 6.63-6.68 (2H, m), 6.75 (4H, m), 6.94-7.0 (2H, m), 7.1-7.3 (2H, m), 8.06-8.11 (2H, m)									
143.				COOH	O	1	1	1	462	50
	^{1}H: 3.77 (3H, s), 3.98 (1H, s), 4.03 (1H, s), 4.53 (1H, s), 4.65 (1H, s), 5.39 (2H, s), 6.90 (2H d, J=8.98 Hz), 7.0 (2H, d, J=8.94 Hz), 7.08 (2H, t, J =8.49 Hz), 7.29 (2H, d, J=8.91 Hz), 7.39-7.43 (2H, m), 7.63 (1H, d, J=6.95 Hz) , 7.7 (1H, d, J=6.95 Hz)									
144.				COOH	O	2	1	1	534	45
	^{1}H: 2.23 (3H, s), 2.39 (3H, s), 3.55 (3H, s), 3.77 (2H, s), 3.93 (2H, t, J=5.64 Hz), 4.21 (2H, t, J=5.95 Hz), 4.36 (1H, s), 4.43 (1H, s), 5.85 (1H, d, J=2.94 Hz), 6.13 (1H, d, J=3.39 Hz), 6.52-6.68 (6H, m), 6.73 (1H, d, J=3.33 Hz), 6.84 (2H, d, J=8.46 Hz), 6.91 (1H, d, J=3.57 Hz).									
145.				COOH	O	2	1	1	560	97
	CD_3OD, ^{1}H: 2.3 (3H, s), 2.46 (3H, s), 3.77 (3H, s), 3.83 (2H, s), 3.96 (2H, t, J=5.6Hz), 4.31 (2H, t, J=5.6 Hz), 4.5 (1H, s), 4.6 (1H, s), 5.85 (1H, d, J=3.3 Hz), 5.97 (1H, d, J=3.3 Hz), 6.6 (2H, m), 6.8 (3H, m), 7.0 (2H, m), 7.15 (1H, m), 7.25 (4H, m).									

Preparation 11

L-Arginine salt of {Benzyl-[3-(3-phenothiazin-10-yl-propoxy)-benzyl]-amino}-acetic acid. (compound No. 146).



To a solution of {Benzyl-[3-(3-phenothiazin-10-yl-propoxy)-benzyl]-amino}-acetic acid. (compound No. 88) (100 mg) in ethanol (10 mL) heated to 60 ^{0}C was added another solution of L-arginine (34 mg) in water (0.2 mL) and the reaction mixture was heated to reflux for 3 hours. Solvent was evaporated under reduced pressure and the residue was triturated with ethyl acetate to obtain 80 mg of product.

Preparation 12

Sodium and potassium salts of the compounds in table 3 were prepared by following the general procedure described below.

To a solution of carboxylic acid (mentioned in table 3) (1 mmol) in alcoholic solvent like methanol, ethanol and the like was added another solution of sodium or potassium alkoxides (0.95 mmol) in alcoholic solvent and the reaction mixture was stirred for 3 hours at 25-30 ^{0}C. Solvent was evaporated and the residue was triturated with dry diethyl ether or diisopropyl ether to obtain the salt of the corresponding carboxylic acid.

The compounds of the present invention lowered triglyceride, total cholesterol, LDL, VLDL and increased HDL and lowered serum glucose levels. This was demonstrated by *in vivo* animal experiments.

A) Demonstration of *in vivo* efficacy of compounds:

i) Serum triglyceride and total cholesterol lowering activity in Swiss albino mice:

Male Swiss albino mice (SAM) were bred in Zydus animal house. All these animals were maintained under 12 hour light and dark cycle at 25±1 °C. Animals were given standard laboratory chow (NIN, Hyderabad, India) and water ad libitum. SAM of 20-30 g body weight range was used. The protocol approved by Institutional Animal Ethics Committee is being used.

The test compounds were administered orally to Swiss albino mice at 0.001 to 50 mg / kg/ day dose for 6 days. The compound was administered after suspending it in 0.25 %

CMC or dissolving it in water, when compound is water-soluble. Control mice were treated with vehicle (0.25 % of Carboxymethylcellulose; dose 10 ml/kg).

The blood samples were collected on 0^{th} day and in fed state 1 hour after drug administration on 6^{th} day of the treatment. The blood was collected in non heparinised capillary and the serum was analyzed for triglyceride and total cholesterol (Wieland, O. Methods of Enzymatic analysis. Bergermeyer, H., O., Ed., 1963. 211-214; Trinder, P. Ann. Clin. Biochem. 1969. 6: 24-27). Measurement of serum triglyceride and total cholesterol was done using commercial kits (Zydus-Cadila, Pathline, Ahmedabad, India).

Formula for calculation:

Percentage reduction in triglycerides/total cholesterol were calculated according to the formula:

Percentage reduction (%) =

$$1 - \left[\frac{TT/OT}{TC/OC}\right] \times 100$$

OC = Zero day control group value OT = Zero day treated group value

TC = Test day control group TT = Test day treated group

Table 1:

Triglyceride lowering activity in Swiss albino mice:

Example No.	Dose (mg/kg/day)	% Triglyceride lowering
113	10	43
122	10	35
130	3	38

ii) Serum glucose lowering activity in db/db mice models

Homozygous animal C_{57}BL/KsJ-db/db mice are obese, hyperglycemic, hyperinsulinemic and insulin resistant (J. Clin. Invest., 85, 962-967, 1990), whereas

heterozygous are lean and normoglycemic. The homozygous animals very closely mimic the human type II diabetes when blood sugar levels are not sufficiently controlled. Since this type of model resembles human type II diabetes mellitus, the compounds of the invention were tested for their antidiabetic activity in this model.

The compounds of the present invention showed serum glucose and triglycerides lowering activities.

Male C_{57} BL/KsJ-db/db mice of 8 to 14 weeks age, having body weight range of 40 to 60 grams, procured from the Jackson Laboratory, USA, were used in the experiment as per the protocol approved by the Institutional Animal Ethics Committee.

Test compounds were suspended on 0.25% carboxymethyl cellulose or dissolved in water when the compound is water soluble and administered to test group containing 6 animals at a dose of 0.001 mg to 50 mg/kg through oral gavage daily for 6 days. The control group received vehicle (dose 10 ml/kg). On the 6^{th} day, one hour after the drug dosing, blood was collected from retro-orbital sinus and the serum was analyzed for glucose and triglycerides were measured using commercial kits (Zydus-Cadila, Pathline, Ahmedabad, India). The serum glucose and triglyceride lowering activities of the test compound was calculated according of the formula:

Serum glucose lowering activity (%) =

$$1 - \left[\frac{TT/OT}{TC/OC}\right] \text{ X } 100$$

OC = Zero day control group value OT = Zero day treated group value

TC = Test day control group TT = Test day treated group

Example No.	Dose (mg/kg/day)	Serum Glucose reduction (%)	Plasma TG reduction (%)
106	3	57	-

No adverse effects were observed for any of the mentioned compounds of invention. The compounds of the present invention showed good serum glucose, lipid and cholesterol

lowering activity in the experimental animals used. These compounds are useful for the testing / prophylaxis of diseases caused by hyperlipidemia, hypercholesterolemia, hyperinsulinemia, hyperglycemia such as NIDDM, cardiovascular diseases, stroke, hypertension, obesity since such diseases are interlinked to each other.